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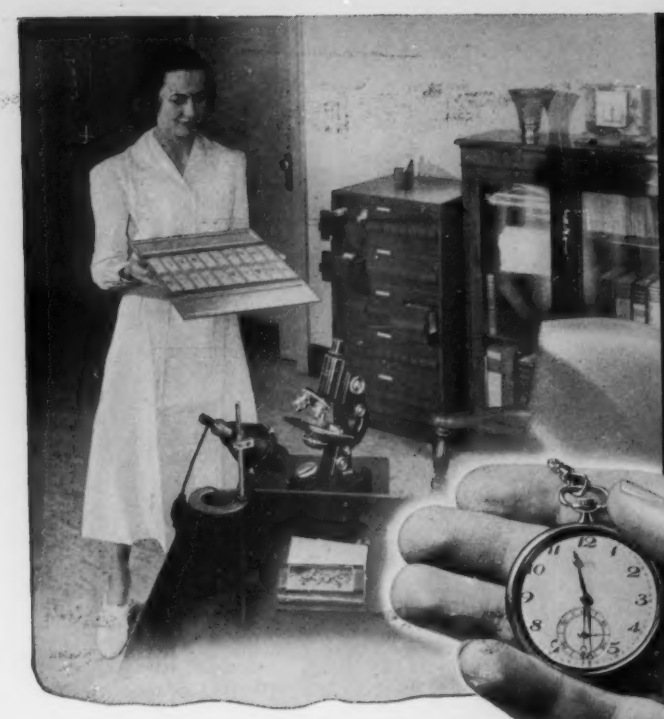

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Scientific Manpower

THE debates, the formulation of plans, are about over. Now it is up to Congress what the nation will do about the training and utilization of scientific, technical, and engineering manpower.

M. H. Trytten's six advisory committees to Selective Service made two proposals designed to provide a continuing flow of trained men for either war or partial mobilization: (*a*) Those youths with the highest aptitude for college training, as determined by tests, should have their military service postponed until their training is over; (*b*) no effort should be made to direct what these young men should study, because no satisfactory determination can be made as to what will be essential to national defense five to ten years from now.

Directly opposed to those proposals was James B. Conant's idea that all eighteen-year-olds should be put into service for two years. That proposal is already dying of its own oversimplicity.

What is now emerging, and what Congress is likely to accept, is a compromise of the two plans. The final product will recognize both the cold hard facts on which the Trytten proposals were based and the political appeal of the Conant plan. That compromise has taken solid shape in the testimony of Assistant Secretary of Defense Anna Rosenberg before the Senate Preparedness Subcommittee. This includes plans to continue some college deferments and to send some 50,000 draftees to college each year. Federal scholarships for qualified students needing them are also suggested. The National Securities Resources Board's Scientific Manpower Advisory Committee is coming out with a similar plan.

The essence of the compromise is that qualified men shall be sent back to college once they have been drafted. It is due to the work of Dr. Trytten and his committees that there is such a wide acceptance of the necessity for such a step. Most important, the unanimous report of the Thomas Committee demonstrates that it has support from two proponents of all-out service who are members of the committee—Vannevar Bush and Gordon Gray, president of the University of North Carolina.

The second Trytten principle—that the student should be allowed to choose what he shall study—has also fallen by the wayside. But, once again, it is likely that, because of the Trytten report, the widest possible interpretation of what is "essential" will be made.

Pulling and hauling now will take place on two issues: (*a*) By what method shall these boys be returned to college? (*b*) Who shall decide what they will study? Former proponents of the Trytten plan will probably want qualified boys, furloughed immediately after induction, to go to colleges of their choice, and a civilian board to decide essential fields of training and see to it that they keep up in their marks. The other extreme is that the boys be members of military units established on college campuses, and that their lives and what they study be strictly regulated by the Defense Department.

It is expected that, either in the new draft law or in the hearings during which the law is written, the intent of Congress that provisions must be made for scientific, technical, and engineering training will be enunciated. Congress will also have to face the problem of utilization of scientific, technical, and engineering personnel already trained. Most plans—and there have been many—visualize compulsory registration of scientific manpower and machinery to place that manpower where it is needed, and to determine how far down in the educational scale such registration should go, and whether placement power should be restricted to the needs of the military or spread over our whole economy. There are few clues as to the thinking of Congress, but the Gurney Bill, under which some doctors can be drafted, may set the precedent.

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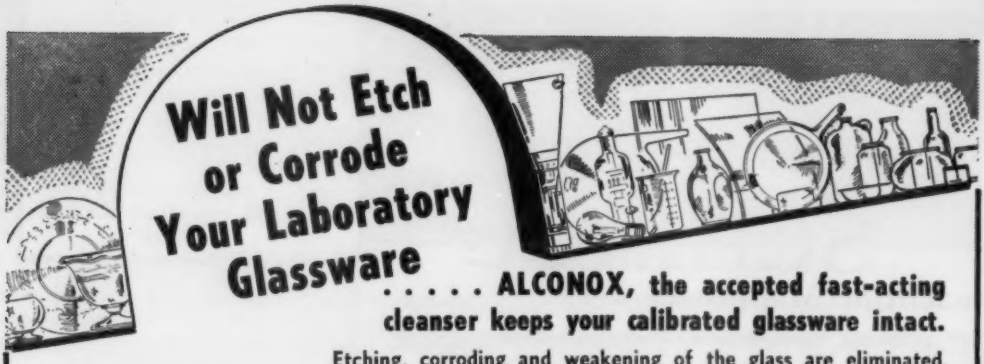

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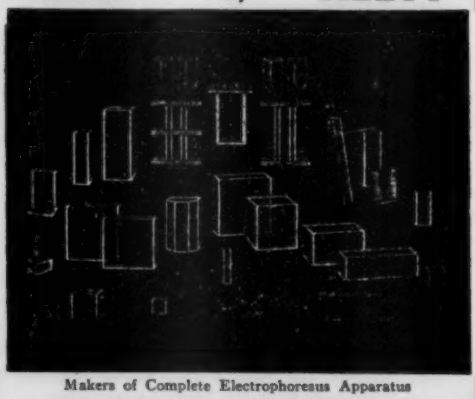

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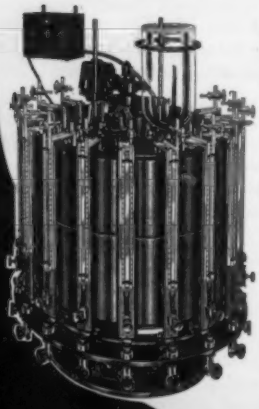

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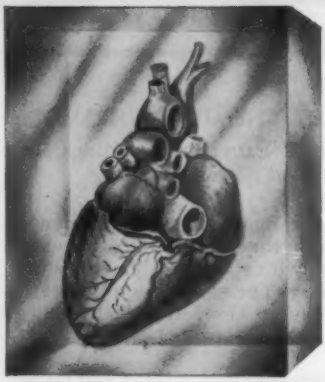

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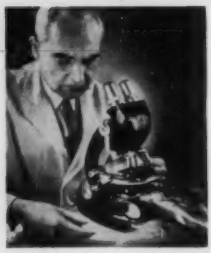

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Principles of Infrared Spectrophotometry

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ALTHOUGH THE INFRARED FIELD was later than either ultraviolet or visible in having a commercially available spectrometer, it is now in a peculiar position with respect to spectrophotometry. In this article spectrophotometry implies the automatic comparison of the spectral power in two radiation beams—an I_0, or reference, beam and an I, or sample, beam. Whereas ultraviolet and visible together have only two types[1] of commercially available spectrophotometers, infrared alone has two, and a third one is under consideration. All three types are different in basic principle.

None of these types is original with the manufacturer—two, at least, were known before commercial production begun. One would therefore conclude that no principle is completely superior to the others—that each has certain inherent advantages and disadvantages whose relative weights influenced the makers' choice. Under such circumstances, a potential user must consider the implications of each principle very carefully in studying the performance of the various instruments. The advantages and disadvantages of the principles are not readily apparent in a description of the instruments alone, primarily because infrared techniques are applicable to such a wide range of problems.

The three principles of infrared spectrophotometry may be described as the memory standardization, the optical null, and the direct ratio. It is not the purpose here to give more than very brief descriptions of the methods, since full detail is available in the literature or from the manufacturers.

System A. *Memory standardization* (*1, 2*). A single beam instrument is used, and an I_0 spectrum is run. A chosen characteristic of the I_0 run is recorded and played back during the I (sample) run to provide the comparison. In the Beckman instruments, the slits are servo-operated during the I_0 run to give a constant radiation signal. The slit schedule is recorded on a magnetic tape, which is played back to control the slits for the I run.

System B. *Optical null* (*3–7*). Two separate radiation beams are taken from the same source, split in space, rejoined at a 180° rotating sector mirror, and passed through the spectrometer proper on alternate half cycles. The sample is placed in one beam, and a balance cell, if required, in the reference beam. If the radiation from the sample beam is different from that of the reference beam, an a.c. signal results from the detector. This signal is used to drive a wedged diaphragm in the reference beam to restore radiation balance or optical null. The position of the diaphragm is recorded continuously as a comparison of the two beams.

System C. *Direct ratio*[2] (*8, 9*). Again two radiation beams, reference and sample, are taken from the source, but essentially 90° radiation-chopping is employed—i.e., each beam is measured with shutter in and shutter out. The two net radiation signals that result from the detector are obtained separately. The I_0 electrical signal is placed across the slide wire of a recording potentiometer, and the I signal is fed at the conventional point, so that an automatic ratio of the two signals is obtained.

Comparison of the three systems is presented in Table 1. Instrument characteristics are shown in the left-hand column. Plus and minus signs are used merely to show with which method the advantages seem to lie. It is emphasized that these are advantages in principle only, and not in performance of the instruments available. It may well occur that a manufacturer, at disadvantage in a certain characteristic, may solve the problem so successfully that his performance in that regard may be superior to the others.

With reference to the first two characteristics of Table 1, comparison is based on single-beam a.c. operation as unity in each respect, although the single beam does not give results equivalent to the beam comparison systems. The noise to signal comparisons are only approximate; actually, even with the assumption of instantaneous detector response, there is a small difference between the instruments of references (*8*) and (*9*) of system C. In reference (*9*) there may be some further signal loss as a function of detector response because of the complete 90° on-off chopping. Similarly, the signal of system D can be more than twice the standard chosen. In system A the noise varies from the $\sqrt{2}$ to 1 from 100–0 per cent

[1] An instrument supplied by the Applied Physics Laboratories for use in ultraviolet or visible is based on a different principle from the General Electric visible spectrophotometer.

[2] In the Savitsky conversion, the radiation beams are not widely separated in space, so that sampling restrictions are involved. This is not considered in the general arguments given here, since it is not inherent in the principle.

TABLE 1

COMPARISON OF METHODS OF INFRARED SPECTROPHOTOMETRY

Requirements or characteristic	System A (memory standardization)	System B (optical null)	System C (direct ratio)	System D (single-beam d.c.)	Standard (single-beam a.c.)
1 Noise	$\sqrt{2}-1$	1	$2\sqrt{2}-2$	½	1
2 Recording time	$2 \rightarrow 1$	1	1	1	1
3 Net radiation measured	+	−	+	−−	+
4 Amplification	−−	++	+		
5 Source stability	−−	+	+		
6 Optical	++	−−	−		
7 Atmospheric interference	−	+	+		
8 Slit mechanism	−	+	+		
9 Sampling	+−	−+	−+		
10 Elasticity (double beam)	−	+	+		
11 Elasticity (single beam)	+	−	−		

transmission, because two independent signals are compared. In system B the noise is unity, provided the filtering blocks noise frequencies greater than the response time of the servo-balance system. The noise of C is twice that of A, since the radiation is measured only half the time. For single-beam d.c., the noise-to-signal ratio is about ½, or somewhat less, since total radiation is used. For one spectrum the recording time for system A is twice that of the single beam standard, because unit time is required for the I_o as well as the I run. However, the time factor of two can approach one if instrument conditions are maintained constant, so that a single I_o run can be used for many I runs. In B and C the recording time is unity. Row one can be converted to unity if the values of row two are multiplied by the square of the respective noise values. Under normal conditions of spectral recording and instrument variation, the factor of $\sqrt{2}$ in noise is probably not appreciable. However, the noise increase of system C will probably be noticeable.

In system B the net radiation is not measured. It is assumed that the source zero radiation condition is the same in either beam, and an explicit zero radiation value is not measured. This assumption is valid if the sampling temperature condition in each beam is approximately the same as the detector temperature. Although this is true for normal work, system B would give slightly erroneous results for liquid-air or high-temperature samples. The error could be measured independently and a correction applied, but in so doing the time advantage of the system is lost. In system D the radiation zero can be measured only at the beginning and end of each spectral region and must be assumed in between. This disadvantage more than balances the noise advantage of the system for most purposes and is the reason d.c. recording is not commonly used today. The lack of a net radiation measurement also implies that the I_o signal is not available for servo-control of operating variables such as slit width, speed of recording, or electrical filtering.

The requirements on amplifier linearity and gain stability, as well as source stability, are very stringent in system A. These characteristics must be maintained very accurately over a period of one-half to one hour for a single spectrum, and for considerably longer if one I_o run is to be used successively. In system B the amplifier has only to detect a null. Similarly, the source must maintain appreciable stability only over a time long compared to the sector-mirror period. In C, amplifier linearity must be good, but gain and source stability conditions are the same as for B. The linearity requirement could be eliminated if the system were operated on an electrical null condition before the amplifier and the ratio of the bucking signals obtained.

In optical requirements the situation is reversed. All the advantage lies with system A. In systems B and C, where split optical paths are used, reflection and scattering characteristics must be maintained constant in each beam. This is very difficult because of the nature of infrared transmitting windows and the number of octaves in the spectral region. System B has an added disadvantage over C in that, for both transmission accuracy and reproducibility, the balance comb or wedge must be accurately linear, and the radiation distribution across it must remain uniform and constant. If the comb is placed at a point conjugate to the source, radiation distribution over the source must remain constant, and there is necessarily a very small but unavoidable error as a function of slit width at very low transmissions. At such a position it is also conjugate to the slits, which introduce dangers from slit jaw irregularities and diffraction effects at very small slit widths. If it is placed at an aperture stop, the reflecting surface of all collimating or condensing mirrors must stay uniform.

In fact, the reversals of advantages 4 and 5 versus 6 are probably the greatest weights in the manufacturers' choice, and considerable experience will be required to decide the validity of the choice.

If atmospheric interference is present, the advantage is with B and C. Careful optical alignment is required to eliminate these effects, but once it is achieved, it is independent of atmospheric changes. This also eases the instrument desiccation problem considerably. In system A atmospheric interference changes imply a new I_o.

The requirements on the slit mechanism are also more stringent in A than in B or C. The slit schedule in A must repeat accurately from I_o to I run, whereas in B or C it must be held only close enough to maintain reasonably constant I_o energy and not change the resolution appreciably.

In sampling, the advantages are mixed and often

depend on the nature of the work. For gas or dilute solutions the same sample cell can be used in both I_o and I runs in system A. The time factor for the two runs must be considered. If the sampling is repetitive, the advantage is clear. If the sampling is highly varied, systems B and C would require the same time to make a blank run as system A requires for the I_o run. However, if the blank run shows that correction to the sample run is required, such a correction is not automatic and may be very tedious. If the blank runs are not necessary as a correction, the time advantage is with B and C. For pure liquid runs, the blank is not the empty cell but a single double thickness plate. Here the advantage is with B and C, unless a large number of runs is involved. In the one case of differential spectra, where one wishes to balance out a component present to 95 per cent or less, system A is at a disadvantage in varied work. Under such conditions the same cell cannot be used, because the component to be balanced will not have the same net thickness in each case. The thickness difference can be made up by a material that has no absorption, but this is possible over only limited spectral regions. The use of cells of different thickness is difficult, particularly if the net thickness contribution of the component to be balanced cannot be controlled—i.e., balancing out the major component of an unknown to study the minors. Such cases are best handled by use of a variable thickness cell in the reference beam and by study of several absorption bands of the major to determine the best compensation thickness. Adjustment of the cell in system A for an unknown sampling would require multiple measurements of I_o and I values at the absorption points.

The double beam elasticity—i.e., simultaneous beam comparison—of systems B and C is the advantage that is involved in the last point of differential sampling. This advantage is also apparent in a case where a spectrum is scanned with a given set of instrument variables, say, for a survey run. If a certain region is desired under different trial conditions, systems B and C can be reset immediately. System A requires changing the I_o tapes or perhaps running new ones. On the other hand, systems B and C lack single-beam elasticity. The requirement that the split optical portions remain matched precludes ease of special work, such as changing the sample beam for some particular problem.

These would seem to be the major comparisons in principle among the three systems. It is also of interest to compare certain of the design features of the Beckman memory standardization instruments and the Perkin-Elmer optical null instrument. Each has provided a rather wide range of control of the various operating variables, as well as camming systems to furnish spectra linear in λ, ν, etc. Beckman has made the scanning speed proportional to the slit width and has chosen to servo the slit widths in the I_o run to provide a constant energy signal versus wavelength. This slit schedule is repeated in the I run. Perkin-Elmer provides a speed suppression feature that permits partial control over scanning speed as a function of radiation beam off balance. Essentially, the mechanism provides a scanning rate as set for regions of no spectral absorption, and automatic slowing of the rate where absorption bands are present. For the slits, Perkin-Elmer has chosen a series of slit-width schedules which provide reasonably constant I_o energy to the servo, and which differ from each other by successive factors of $\sqrt{2}$. Again, once these design features are set, comparisons in principle are possible, although the resultant spectral effects must be studied experimentally for any decisions.

The Beckman rate of scan feature is very attractive, since it provides automatically controlled, optimum rate of scanning for information that may be present in each spectral region so long as I_o versus λ is a reasonably smooth function. The Perkin-Elmer suppression, on the other hand, permits some speed discrimination, dependent on whether the information in a region is of interest. A combination of the two features would be highly desirable. A decision between each alone is difficult, unless they could be compared on the same instrument. The Perkin-Elmer feature is more apparent for rapid scanning and loses its effectiveness at slower scanning rates. The Beckman scanning method would ensure the same scanning time on either a wavelength or wave-number basis. This, combined with the decision to servo the slits, makes their prism interchange easier in principle, since Perkin-Elmer must interchange both slit and wavelength cams, whereas Beckman must change only the wavelength cam.

The Beckman decision to servo the slits implies the disadvantage in solution runs that the spectral resolution schedule for a solute would be a function of the solvent thickness used, since the I_o slit schedule would vary with solvent thickness. A chemical mixture is often more soluble in a given solvent than its pure components. Minimum solvent thickness is usually desirable, but it might be difficult to obtain pure spectra under the same solvent slit schedule as would be desired for the mixture. Similarly, there would be a change in resolution schedule in the Beckman with appreciable atmospheric absorption. A similar effect might be observed in the Perkin-Elmer with rapid scanning, as strong atmospheric absorption would alter the gain in the servo loop and make the response sluggish. In the water region, at least, because of the narrow band widths, these effects would not be noticeable in either system with normal samples.

Each instrument seems to be at a disadvantage in differential spectral running where one wishes to obtain a valid spectrum of a solute in a spectral region of high solvent absorption. In the Perkin-Elmer the desired slit-width schedule is chosen and the amplifier gain increased, so that the product of available I_o signal times gain is sufficient for the servo system. To

reduce the noise resultant from the high gain, the instrument response time must be increased and scanning speed must be reduced to permit following the spectral structure. With the scanning speed so set, the instrument is operating inefficiently in the regions of high solvent transmission, since it is running more slowly than necessary.

The same situation holds in the Beckman. With a certain resolution desired at the bottom of a solvent band, the energy available is fixed and, therefore, the signal value by which the slit program is determined. In regions of high solvent transmission the slit must narrow to maintain this constant. Since scanning rate is a function of slit width, the instrument will scan more slowly than necessary through the latter regions, although spectral resolution would be increased.

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Comments on "Principles of Infrared Spectrophotometry"

VAN ZANDT WILLIAMS very kindly submitted a draft of his paper to us for comment prior to publication. Although in many respects we have come to full agreement with Dr. Williams, and we appreciate and respect his sincere effort to present a judicial consideration of the instrument problem, there remain certain irreconcilable differences in point of view between us.

One such issue concerns the respective time and noise efficiencies of the instrumental systems. A spectrophotometer is used to collect data. Whether these data are truly "per cent transmission" can only be determined by making a standardizing run as well as a sample scan, as Dr. Williams recognizes in his discussion of the sampling problem. The true per cent transmission is the quotient of these independent values, hence "noise" in both runs contributes to errors in actual values of per cent transmission. Furthermore, to be accurate, data must include matching corrections. These considerations are valid for any spectrophotometric system used in any wavelength region. In the infrared, however, they are of unusual importance, because of the magnitude of the noise problem and the impermanence of common optical materials.

The distinctions between systems A and B in respect to noise and recording time are therefore these: records made with system B do not contain the standardizing information and, consequently, may have lower noise, but they represent per cent transmission only approximately. System A provides a slightly "noisier," but direct-reading, record. Any method that can be proposed for modifying system B to provide actual per cent transmission records increases its noise level. Also, in principle, to obtain equally reliable per cent transmission data with either system, the same number of scans is required. The application of these ideas to the other systems is obvious.

The problems of amplifier linearity and stability and of source stability are admittedly important for system A. We feel, however, that even greater emphasis should be placed on the alternative difficulties encountered in system B in obtaining linearity and achromatism of the beam attenuator. We also feel that it is relevant to point out that the required high order of amplifier stability and linearity and of source stability can be obtained by straightforward application of recognized techniques in electronic engineering. Fortunately, stability and linearity need not depend upon nice mechanical adjustment or perfection of construction of components, but may be inherent in design. The validity of these statements has been tested in a commercial infrared spectrophotometer for almost five years.

Another significant distinction between system A and those remaining is that the former requires far more precise control of monochromator temperature, in order to achieve the extreme wavelength stability needed to retain compensation of sharp background absorption bands at high resolution. Experience has shown that this difference is of considerably greater importance than most of those formerly emphasized.

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Technical Papers

The Magnetic Susceptibility of Vitamin B_{12} and B_{12b}

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It has been stated by Rickes, Brink, Konivszy, Wood, and Folkers (*1*) that vitamin B_{12} probably is a hexacoordinated cobalt complex, although these authors do not cite the experimental evidence on which this conclusion is based.

Magnetic measurements on pure samples of vitamin B_{12} and related cobalt compounds may be expected to yield unambiguous evidence concerning the nature of the bonding of the cobalt moiety of these substances. We have available an apparatus for measuring the magnetic susceptibilities of very small samples of solid compounds (*2*). Through the courtesy of various pharmaceutical laboratories, we have been supplied with samples of vitamin B_{12} and B_{12b} in quantities sufficient for magnetic measurements.

The susceptibilities were measured by a modification of the Faraday method, using a sensitive quartz fiber torsion balance to measure the magnetic forces and a 5-in. alnico permanent magnet, with pole pieces especially cut to provide a small region of uniform dH/dx. Since neither the field strength nor its rate of change in the experimental region was known accurately, our measurements are comparative and refer in all cases to the behavior of the test samples as compared with that of samples of reagent grade $FeSO_4(NH_4)_2SO_4 \cdot 6H_2O$ under the same experimental conditions. In computing our results, we have taken the value of χ for our reference standard to be 29.45×10^{-6} cgs units. All measurements were made at room temperature and in air. No corrections were made for the influence of the slight susceptibility of the surrounding air, since these corrections were, in general, of a smaller order of magnitude than the experimental error of the measurements themselves.

In all cases in which the quantity of sample was sufficient, at least two portions of the same preparation were investigated separately. This served as a test both for magnetic homogeneity of a particular preparation and to reveal any significant contamination with magnetically active material resulting from our own handling of a sample in preparation for a run.

The results of our measurements are summarized in Table 1.

Of the 6 preparations of vitamin B_{12} examined by us, 3 (Upjohn samples 223-WGJ-6, 249-WGJ-7, and 247-WGJ-7) were clearly diamagnetic and are unquestionably covalent cobaltic complexes with octahedral d^2sp^3 bonding.

TABLE 1

MAGNETIC SUSCEPTIBILITIES OF VARIOUS SAMPLES OF VITAMIN B_{12} AND B_{12b}

Compound	Source	Run No.	Sample Wt (mg)	χ (cgs $\times 10^6$)	χ_m Mol Wt = 1490 (*3*)	μ_{eff} (Bohr Magnetons)	Remarks
B_{12}	A	1	0.41	−0.69			
B_{12}	A	2	.50	−0.69			
B_{12}	B	1	.15	Diamagnetic (−)			Sample too small for accurate measurement
B_{12}	C	1	.25	−0.63			
B_{12}	C	2	.15	Diamagnetic (−)			Sample too small for accurate measurement
B_{12}	D	1–3		Variable paramagnetism (+)			Samples inhomogeneous
B_{12}	E	1	.72	+5.88	+8760	4.45	
B_{12}	E	2	.40	+5.83	+8690	4.45	
B_{12}	E	3	.40	+5.40	+8050	4.36	
B_{12}	F	1	.40	−1.17			
	F	2	.39	+1.01			
B_{12b}	G	1	.47	−0.70			
B_{12b}	G	2	.57	−0.54			
B_{12b}	H	1	0.33	+0.30			
B_{12b}	I	1–2		Variable paramagnetism (+)			Samples inhomogeneous

A. The Upjohn Company, Research Laboratories, Kalamazoo, Mich., Vitamin B_{12}, No. 223-WGJ-6.
B. *Idem.*, No. 249-WGJ-7 (Merck lot #9R-6537).
C. *Idem.*, No. 247-WGJ-7.
D. British Drug Houses, Ltd., London, Eng.
E. Merck & Co., Inc., Rahway, N. J., Vitamin B_{12}, No. 9R-5,168.
F. Lederle Laboratories Division, Pearl River, N. Y., Vitamin B_{12}, No. NP-86-8-1.
G. The Upjohn Company, Research Laboratories, Vitamin B_{12b}, No. 233-WGJ-7.
H. *Idem.*, No. 239-WGJ-7.
I. Lederle Laboratories Division, Vitamin B_{12b}, No. NP-92-184-7.

The Lederle sample (NP-86-8-1) exhibited both diamagnetic and paramagnetic behavior. Since the sample appeared homogeneous we conclude that the paramagnetism is due to some slight impurity and that the pure B_{12} is a covalent cobaltic complex.

Two preparations (British Drug House and Merck 9R-5168) showed paramagnetic behavior. The British Drug Houses preparation as received by us in a sealed glass tube was visibly inhomogeneous; it was evident that a part of the sample had been charred in sealing

the tube. Since charring would be expected to produce a mixture of carbon and strongly paramagnetic cobaltous phosphate, we attach no significance to either the sign or magnitude of the susceptibility of this preparation.

The Merck preparation appeared to be homogeneous and gave consistent results on repeated measurement. The Bohr magneton number of this material, calculated from the susceptibility after correcting for the diamagnetic contribution of the remainder of the molecule, is in fairly good agreement with that expected for an ionic compound of Co^{II}. However, the variable orbital contribution found in different cobaltous compounds somewhat diminishes the significance of the exact magnitude of the magneton number.

In spite of the agreement between different runs on this material and the fact that the susceptibility is quite consistent with that expected for an ionic Co^{II} compound, we are inclined to suspect that this result is due to uniform contamination with a small amount of strongly paramagnetic or ferromagnetic impurity. Since we are not equipped to measure the field strength dependence of the susceptibility, the last-mentioned possibility could not be investigated experimentally. The question as to whether vitamin B_{12} may exist in one form as cobaltous compound undoubtedly justifies further laboratory investigation.

We regard it as significant that the Merck 9R-5168 sample was not obviously different in color or appearance from other samples of B_{12} which were diamagnetic.

Of 3 samples of vitamin B_{12b}, one (Upjohn 233-WGJ-7) was diamagnetic, and consequently must be a hexacoordinated covalent cobaltic complex. Another sample (Upjohn 239-WGJ-7) was available in smaller amount, but one run showed it to exhibit weak paramagnetism. We believe this result probably is due to the presence of a para- or ferromagnetic impurity. The third (Lederle NP-92-184-7) had been charred in sealing the tube, and the erratic paramagnetism is without significance.

In summary, samples of vitamin B_{12} and vitamin B_{12b} have been found to exist in the form of covalent cobaltic complexes with octahedral d^2sp^3 bonding. The possibility that these substances may exist as cobalt compounds exhibiting other types of bonding requires further investigation.

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Some Adsorption Colors and their Significance for Tautomeric and Thermochromic Effects

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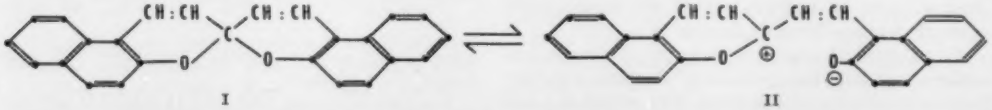
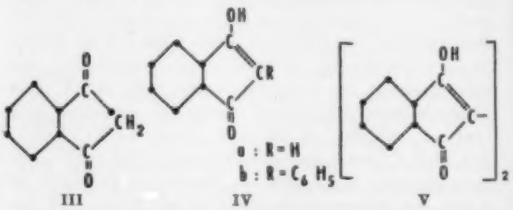
Some spiropyrans are colorless substances which form colorless solutions in cold inert solvents, whereas the hot solutions are intensely colored, e.g., violet-blue in the case of β-dinaphthaspiropyran (I); the phenomenon is reversible. The color change is usually explained by the formation of a heteropolar molecule, betaine (*1*), (compound II).



I II

The correctness of this hypothesis was recently questioned by Hukins and Le Fèvre (*2*), but the proof of the explanation outlined here may be seen from the following experiment. When a piece of activated alumina[1] is added to the cold colorless solution of (I) in xylene, the surface of the colorless alumina becomes bluish-green immediately. Using a column of activated alumina, the adsorbed material may be eluted by means of methyl alcohol. This experiment is reminiscent of the observations by Weitz and coworkers (*3*). It was found that the colorless triaryl-



III IV V

methyl halides and related substances were adsorbed with the color of the corresponding cation or a similar color, e.g., the colorless triphenylmethyl chloride gives the yellow color of the triphenylmethyl cation, and the colorless base $[(CH_3)_2N \cdot C_6H_4]_3C \cdot OH$ is adsorbed with the violet color of the corresponding cation.

In benzene, 1,3-diketohydrindene (III) gives a colorless solution. When a piece of activated alumina is added to a cold solution of (III) in benzene a violet color results at once. It seems that the violet color is due to the enol form (IVa). Compound IVb is dark red (*4*), and V is violet (*5*).

[1] Obtained from Peter Spence and Sons, Ltd., London.

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Hydatid Disease (*Echinococcosis*) in Alaska and the Importance of Rodent Intermediate Hosts

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Hydatid disease, caused by the larval form of a tapeworm, *Echinococcus granulosus* (Batsch, 1786), is of circumpolar distribution, but has not previously been considered to be of much public health significance in North America. It is the purpose of this paper to present observations on this disease in Alaska, with special reference to its transmission to man.

Magath (*1*) reviewed all known North American cases and concluded that most of these had been contracted abroad. Infections in dogs have likewise been considered rare; in his review of the literature, Riley (*2*) could find but one North American record and concluded that wild carnivora and herbivora serve to maintain this parasite in the United States and Canada. Subsequent work has borne out this conclusion. The occurrence of *E. granulosus* in wild animals in North America has been reviewed by McT. Cowan (*4*).

The data derived from intensive parasitological investigations of the mammalian fauna of Alaska, carried on by us over the past two years, indicate that *E. granulosus* is well established in the Territory, in both dogs and wild canids. In arctic Alaska, particularly, where dogs are commonly very closely associated with man, there is unusual opportunity for human exposure to this parasite. The finding of infected dogs in several arctic Eskimo villages (Barrow, Kotzebue, Wainwright, Unalakleet, Anaktuvuk Pass) indicates that potentially, if not actually, a serious human health problem is involved. In addition, we have recorded this parasite from both red and arctic foxes in northern Alaska, and from the wolf over the greater part of the Territory. Moose and caribou apparently serve as the essential intermediate hosts on the mainland, since the examination of several hundred mammals of other species has failed to disclose the larval infection. The practice of the natives of feeding dogs the discarded parts from moose and caribou enhances the possibilities for canine infection.

Although the status of hydatid disease in Alaska is in general poorly known, preliminary studies on St. Lawrence Island have disclosed, through skin tests with nonspecific *Echinococcus* antigen, a high incidence of human reactors. In the villages of Gambell and Savoonga, positive reactions of 20% (126 persons tested) and 28% (106 persons tested), respectively, were obtained. As is usual under native conditions, dogs here are found in close association with man, but not to any greater degree than in arctic Alaska in general.

Fig. 1. Specimen of *Microtus oeconomus* showing location and appearance of larval cysts of *E. granulosus*.

Autopsy of 26 St. Lawrence Island dogs failed to disclose any animals infected with *E. granulosus*. Five of 7 arctic foxes (*Alopex lagopus*), likewise examined, were found to be infected, however. The mammalian fauna of the island is poor as far as land species are concerned. Red foxes (*Vulpes* sp.) are rare, but occur in small numbers. Various rodents are present: tundra vole (*Microtus*), red-backed vole (*Clethrionomys*), lemming (*Dicrostonyx*), ground squirrel (*Citellus*). A shrew (*Sorex*) occurs on St. Lawrence Island, and the reindeer has been introduced. Of these, only the reindeer is an obvious intermediate host for *E. granulosus*. For some years, however, this animal has not been killed for food, since an effort is being made to increase its numbers. In view of this situation, some other explanation for fox infections was necessary.

Schiller, during the summer of 1950, discovered infections of larval *E. granulosus* in the tundra vole, *Microtus oeconomus innuitus* Merriam, and all available evidence indicates that this rodent is the only impor-

tant intermediate host present. Of 385 voles examined by the writers during 1950, nine, or 2%, were infected. During 1949 and 1950, this vole was very abundant, apparently at a cyclic high level of population density, so that, although the relative number of infected voles is small, the actual number may be quite high. The other microtine rodents (*Clethrionomys* and *Dicrostonyx*) were at a low point in their cycle, and specimens could not be collected for study. Eighty-five ground squirrels were examined without finding any larval stage of *E. granulosus*. The larvae in the voles were of typical appearance, and ranged in size from 2 up to 3 cm in diameter (Fig. 1). The liver and mesentery are commonly involved. The effect of this parasite on the intermediate host will be discussed in a future publication.

It is well known that various species of mouselike rodents form the bulk of the diet of the arctic fox. It is also known that, particularly under conditions of high rodent populations (e.g., cyclic "high" of lemmings), dogs feed upon these easily obtained animals. It can be assumed that St. Lawrence Island dogs also might become infected from this source.

Man's association with the arctic fox is ordinarily not intimate enough to allow infection by its parasites. In this case, however, it appears that there might be a relationship that could account, at least in part, for human infections. The St. Lawrence Island people are hunters, depending almost entirely upon the flesh of sea mammals for their subsistence. During the summer months, however, a considerable quantity of a native green plant, as yet unidentified by us, is consumed. This plant is eaten in the field, unwashed and raw, as it comes from the ground. Arctic foxes are so abundant that it can be assumed that there is considerable contamination of the vegetation. It is of interest that Riley (*3*) stated that human cases of hydatid infection may be contracted by eating wild fruits contaminated by eggs from the feces of infected canids.

Not all factors involved in the epidemiology of the human infections are known. Some infections may result from ingesting eggs from the feces of dogs. Although they are perhaps not commonly infected now, it is possible that dogs harbored *E. granulosus* more often in former years when reindeer entered much more into the economy of the people. Reindeer serve as suitable intermediate hosts for this parasite in Alaska (*4*), and, when they were formerly slaughtered for food, waste parts were undoubtedly available to dogs. Organs such as lungs, in which the larval forms of *E. granulosus* often localize, are usually discarded, as would be anything of unusual appearance such as a large hydatid cyst. It is also possible that the water supply could afford opportunity for human infections, since water is obtained from sources open to fecal contamination by dogs and foxes.

Further investigation may disclose that hydatid disease in Alaska constitutes a serious public health hazard. On St. Lawrence Island, at least, in addition to the positive skin reactions, there is considerable clinical evidence of echinococcosis. Although a thorough clinical study of the reactors has not yet been made, there has been some opportunity for incidental observations. During the past two years two patients from the small population of St. Lawrence Island have undergone surgery for the removal of liver abcesses, and one man still has a post-operative draining sinus. Routine examination of various individuals by Alaska Department of Health personnel has indicated presence of an unusual number of nodular livers.

From the work so far, it is concluded that interstate shipment of dogs from arctic America should be prohibited. These investigations are being continued, and it is hoped that further work will disclose the over-all status of echinococcosis in Alaska, and lead to suitable control measures.

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The Effect of Maleic Hydrazide on Certain Dehydrogenases in Tissues of Onion Plants[1]

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Maleic hydrazide in aqueous sprays applied to certain plants inhibits or reduces growth to an extent depending upon the concentration of the spray and the plant species involved. Tomato plants are very sensitive to this chemical. According to Schoene and Hoffman (*1*), the cupric and zinc salts of the acid at 2,000 ppm concentration stopped tomato growth for a period of 2 months, after which growth was resumed. Preliminary tests using the diethanolamine of maleic hydrazide on tomatoes confirmed the observations of Schoene and Hoffman concerning the retardation of growth. Onion bulbs have a much greater tolerance than tomato plants. Several spray applications with concentrations ranging up to 3,000 ppm did not cause necrotic spots on the leaves, and growth differences between the treated plants and the control plants were not visually apparent until 30 days after treatment. Plants treated with the chemical were not kept under observation long enough to ascertain if normal bulb formation would occur.

Since maleic and fumaric acids are isomeric, it was postulated that maleic acid might be interfering with the function of one or more enzymes in the respiration cycle. In order to test this hypothesis the activity of

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several dehydrogenases was determined in tissues of plants treated with various concentrations of maleic hydrazide, using a triphenyltetrazolium chloride technique.

Mattson, Jensen, and Dutcher (*2*) suggested that certain pyridine nucleotide dehydrogenases reduced triphenyltetrazolium chloride to the red water-insoluble formazan. Kun and Abood (*3*) reported that succinic dehydrogenase activity could be determined in rat tissue homogenate by a colorimetric measurement of the amount of formazan formed from the tetrazolium salt at pH 7.4. Mattson and Jensen (*4*) found that reducing sugars could be determined at higher alkalinity by means of this salt. The method used in this study was that of Kun and Abood (*3*), with certain modifications making it suitable for the determination of several dehydrogenases in plant tissue.

Determinations attempted on tomato tissue were not successful, since the chlorophyll present prevented accurate reading in the colorimeter, and a suitable solvent was not found to remove the chlorophyll without inactivating the dehydrogenases. For that reason onion tissues were used, since the bulb and the underground portions were free of chlorophyll. The bulbs (sets 1/2 in. in diameter) were planted in pots, and one lot grown in full sunlight in the greenhouse and another in complete darkness. When the shoots had attained a height of approximately 3 in. they were sprayed with maleic hydrazide solutions in concentrations equivalent to 0 (control), 1,000, 2,000, and 3,000 ppm of the free hydrazide for 3 successive days. The etiolated plants were tested at the end of 7 days, and the green-leaved plants at the end of 20 and 50 days after the first spray application. The entire plant of the etiolated onions was tested, but only the underground chlorophyll-free parts of the green plant were used. The samples were washed in distilled water to free them of soil, cut into small fragments, and ground into a homogeneous mass. Ten average onion bulbs yielded 12 ml of homogenate, to which 4 drops of distilled water was added to reduce slightly the plasticity of the mass.

The reagents used were: the diethanolamine of maleic hydrazide (30% maleic hydrazide) diluted to 1,000, 2,000, 3,000 ppm of the hydrazide; 0.2*M* monopotassium phosphate buffer (pH 7.4); 0.2*M* solutions of sodium succinate, sodium fumarate, sodium malate, and sodium pyruvate, all adjusted to pH 7.4; and 0.2*M* glucose and alcohol solutions. The dye was a freshly prepared 0.1% solution of triphenyltetrazolium chloride. Purified acetone was used as a solvent for the formazan produced.

Each reaction tube contained 0.5 ml of buffer, 0.5 ml of substrate, 1 ml of the tissue homogenate, and 1 ml of triphenyltetrazolium chloride reagent. By trial it was determined that volumetric aliquots of fresh tissue homogenate of both treated and control plants were of similar dry weight. The tubes were placed in a 38° C oven for a period of 20–24 hr, after which 7 ml of acetone was added to dissolve the formazan produced. The solution was filtered to obtain a clear tissue-free solution and read in a Coleman spectrophotometer at 490 mμ. A blank of normal onion tissue homogenate which had been heated to 82° C for 5 min produced no formazan. Likewise, 0.5-ml samples of 1,000, 2,000, 3,000 ppm of the maleic hydrazide solutions did not reduce the tetrazolium salt at pH 7.4. A standard curve was prepared using solutions of 100, 200, 300, and 400 μg of triphenylformazan in acetone.

TABLE 1

MICROGRAMS OF TRIPHENYLFORMAZAN PRODUCED BY DEHYDROGENASES IN ONE ML OF ONION HOMOGENATE IN 20 HR AT 38° C FROM PLANTS TREATED WITH 0, 1,000, 2,000, 3,000 PPM OF MALEIC HYDRAZIDE. TESTED 20 DAYS AND 50 DAYS AFTER FIRST APPLICATION

Substrate	Control	Maleic Hydrazide Concentration		
		1,000 ppm	2,000 ppm	3,000 ppm
		Triphenylformazan in μg		
20 days after first application				
Succinate	190	145	135	130
Fumarate	195	155	125	135
Malate	165	135	135	125
Pyruvate	130	90	90	100
50 days after first application				
Succinate	125	45	20	63
Fumarate	143	33	20	30
Malate	155	33	30	43
Pyruvate	73	30	30	35
Glucose	55	25	40	30
Ethyl alcohol	63	30	20	35

The results obtained from onions treated with maleic hydrazide and grown in full daylight are presented in Table 1, where the quantity of triphenylformazan produced by the several dehydrogenases is indicated. In all samples of onions treated with maleic hydrazide, the amounts of triphenylformazan produced by the dehydrogenases were apparently less than in the untreated samples.

At the time of the 50-day test the leaves of the treated onions were approximately 5 in. shorter than the leaves of the control plants; the roots of the former were about half as long as the roots of the latter, and appeared thicker and less fibrous. The bulbs of the treated plants appeared swollen and

TABLE 2

MICROGRAMS OF TRIPHENYLFORMAZAN PRODUCED BY DEHYDROGENASES IN ONE ML OF ETIOLATED ONION TISSUE HOMOGENATE IN 20 HR AT 38° C FROM PLANTS TREATED WITH 0, 1,000, 2,000, AND 3,000 PPM OF MALEIC HYDRAZIDE. TESTED 7 DAYS AFTER FIRST APPLICATION

Substrate	Control	Maleic Hydrazide Concentration		
		1,000 ppm	2,000 ppm	3,000 ppm
		Triphenylformazan in μg		
Succinate	160	135	10	60
Fumarate	135	165	35	115
Malate	157	5	10	15
Pyruvate	105	10	15	5
Glucose	15	0	0	20
Ethyl alcohol	0	20	15	0

flabby, with air spaces between fleshy leaf sheaths. The proportional reduction in the amount of triphenylformazan produced in the treated samples was more pronounced after 50 days than it was on the twentieth day after treatment.

Table 2 gives the results found with onions grown in the dark and tested on the seventh day after maleic hydrazide treatment. In general the dehydrogenases were less active in the etiolated plants than in the plants that received full sunlight. These plants grew rapidly, and probably the waxy coating on the epidermis was not so thick as that on the plants grown in full sunlight. This condition may have favored the entrance of the chemical into the plant tissue. The 3,000 ppm sprays of maleic hydrazide frequently had less effect on the dehydrogenases than the sprays of 2,000 ppm. This might be attributed to local toxic effects severe enough to retard hydrazide translocation. Morphological differences were not apparent between the treated and control plants.

The results indicate that maleic hydrazide sprayed upon the foliage of plants affects respiration through the partial inactivation or inhibition of one or more of the dehydrogenases. The rapidity of the effects of the chemical apparently are governed by the rate of its absorption into the plant.

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The Effect of Desiccated Thyroid, Iodinated Casein, and Casein on a Rachitogenic Diet

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At Michigan State College a modified Steenbock rachitogenic ration is used for the assay of vitamin D milks. This ration is somewhat goitrogenic, as well as deficient in one of the essential amino acids—namely, lysine. Rats fed the Steenbock ration are found to have thyroid enlargements with hyperplasia. This is to be expected, since the diet on the average has a content of 15 γ iodine/g as determined by Levine, Remington, and von Kolnitz (*1*). The daily intake of iodine necessary to yield a concentration of 1% iodine in the thyroid (dry basis), which is essential to normal thyroid functioning, was found by the same workers (*2*) to be approximately 1γ/day. This same group found that the low-iodine goiter is produced when the iodine content in the gland is 0.03% or less (dry basis), and this corresponds probably to an iodine intake from known sources of 0.3 or 0.4γ/day. Therefore, inasmuch as lack of uniformity in the growth of animals might be due to variations in thyroid activity, it was considered likely that the use of desiccated thyroid or iodinated casein would influence the growth of rats fed the rachitogenic diet and result in more uniform growth. Because desiccated thyroid is expensive and its potency variable, iodinated casein, as prepared by Reineke (*3*), was also used, since it provided a comparatively inexpensive product of nonvariable high-thyroid activity.

With the knowledge of the amino acid requirements of the rat, Francis (*4*) tabulated the amount of the individual essential amino acids present in the Steenbock ration and found it to be deficient in lysine. The addition of 0.5% lysine effectively increased the growth rate in addition to reducing the incidence of respiratory infections. Therefore, a study was also made of the value of adding casein to increase the supply of lysine, one of the limiting amino acids.

Throughout the pre-rickets-producing period the rats were maintained on a diet that provided for normal development in all respects except that the supply of vitamin D was limited so that the rats would develop severe rickets in 21 days. For the rickets-producing period a rachitogenic ration consisting of table corn meal 72%, wheat gluten 20%, yeast 1%, and NaCl 1% was used, as well as the modifications indicated in Table 1.

TABLE 1

Ration No.	Modifications
I.....	Basal (the above ration)
II.....	1 kg basal + 5 gr desiccated thyroid*
III.....	1 kg basal + 10 " " "
IV.....	1 kg basal + 25 " " "
V.....	Basal + 1% iodinated casein
VI.....	Basal + 0.05% " "
VII.....	Basal + .025% " "
VIII.....	Basal + .0125% " "
IX.....	Basal + 0.025% iodinated casein − 5% casein
X.....	Basal + 5% casein

* ½ grain commercial desiccated thyroid tablets were used.

Young albino rats of the Michigan State College strain, weighing from 44 to 60 g and 21–25 days old, were assembled into groups of 2 or 3 and fed the rachitogenic diet or one of the above modifications for 21 days and water, *ad libitum*. They were then placed in separate cages 1 day prior to the beginning of the 10-day assay period, so as to adequately adjust themselves to their new surroundings. The animals received a supplement of homogenized vitamin D milk supplying 4 U.S.P. units of the vitamin. In each series some animals were included as negative controls. At the end of the assay period the animals were killed, and the distal ends of the radii and ulnae removed and cleansed of adhering tissue. The bones were then permitted to remain at least overnight in 95% ethanol; "line tests" were then run.

The criteria employed were growth during the experimental period, general appearance of the lines,

and width of the metaphyses, since these are the factors used in routine assay. The results are indicated in Table 2.

TABLE 2

Ration No.	No. Starting Animals	Av Initial Wt	Weekly Wts 1st	2nd	3rd	Av Wt Gained in 3 Weeks
I	30	48.7	55.9	66.1	74.1	25.4
II	16	49.2	55.4	67.4	81.6	32.4
III	16	47.8	56.4	65.2	72.5	24.7
IV	9	51.8	57.2	72.0	81.8	30
V	10	48.4	55.6	63.4	...	...
VI	13	48.0	53.1	62.6	68.2	20.2
VII	32	47.3	57.6	66.8	78.1	30.8
VIII	14	48.7	56.1	65.3	73.8	25.1
IX	16	51.8	58.7	74.8	88.9	37.1
X	16	47.2	53.1	71.2	79.4	32.2

The figures represent several similar series started at slightly different intervals.

(*a*) During the depletion period the following rats died: 1 each on rations III and VII; 10 on ration V; and 5 on ration VI. (*b*) During the assay period the following rats died: 1 each on rations II and VIII; 2 each on rations I, III, IX, and X; 3 on ration IV; and 4 each on rations VI and VII.

All rachitic metaphyses were of desirable width and character.

Line test results:

a) Rats on rations I and VIII produced medium to thin lines.

b) Rats on rations III, IV, and VI produced thin high lines.

c) Rats on rations II, VII, and IX produced uniform medium lines.

d) Rats on ration X produced lines varying from medium to diffuse.

From the data it is evident that rations III, IV, V, and VI are unsuitable for the standard 21-day period. This may be attributed to an excessive intake of desiccated thyroid or iodinated casein. The detrimental effects assert themselves usually within 2–4 weeks, as evidenced by the number of rats that died during the rickets-producing and assay periods and by the high thin line of calcification, which is usually the result of insufficient food consumption.

The addition of 5 grains of desiccated thyroid to the basal ration produced the best growth, as well as the most uniform lines, when compared with the rest of the respective series. Rations VII and I appear about equal in their ability to promote growth; however, the addition of 0.025% iodinated casein appears to aid definitely in calcification response. Each series of rats received Michigan State College homogenized vitamin D milk calculated to supply 4 U.S.P. units vitamin D. Some variation in the actual potency of vitamin D milks might, of course, be expected. A series containing rats fed 0.025% iodinated casein, 0.0125% iodinated casein, as well as plain basal, were fed milk of somewhat lower vitamin D content because the line test responses were generally smaller. Nevertheless, those receiving ration VII showed better responses.

The fact that rats on ration II seem to do better than rats on ration VII is quite interesting since apparently both represent optimum tolerable levels of desiccated thyroid and iodinated casein. The possibility exists that the thyroid extract may differ somewhat in its over-all physiological activity from that of the iodinated protein.

The results with ration VIII containing 0.0125% iodinated casein indicated that this amount of iodinated casein did not affect the animals with regard to rickets production and the line test.

In no case did the average gain in weight in 3 weeks of rats receiving either ration II or VII exceed the respective basal group by more than 7 g. This may be attributed to the fact that the basal ration is deficient in lysine as well as available phosphorus, thus limiting the effect of either the iodinated casein or desiccated thyroid as growth stimulators. When rations IX and X were employed, the growth rate was greatly increased over the corresponding basal fed group. Furthermore, the incidence of respiratory ailments was greatly reduced by the addition of casein to the ration, thereby providing greater economy in animal usage. The growth attained by the end of the first two weeks was sufficient to suggest that only a two-week period would be necessary for the preparation of rats for vitamin D assays. The results, therefore, compare favorably with those obtained with lysine. The line test results, using rations IX and X, further substantiate the effectiveness of iodinated casein in producing more uniform lines.

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Screening of Potential Cancer-inhibiting Agents[1]

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Fildes (*1*) in 1940 stated that modified essential metabolites should be sufficiently closely related to the essential metabolites on which they are based as to fit the same enzyme, but sufficiently different to be devoid of essential metabolic activity.

Since various investigators (*2*) had reported that the concentration of nucleic acids in tumor-bearing animals is greater than in normal animals, it was apparent that adenine and guanine inhibitors might be found which would retard tumor growth, without ad-

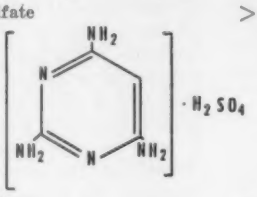
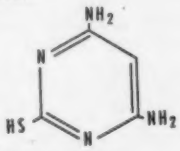
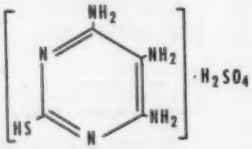
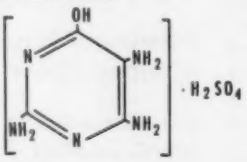
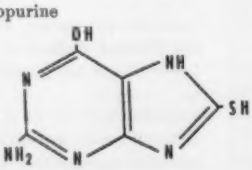
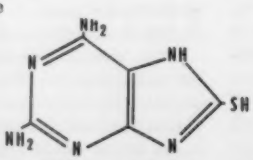
[1] The work described in this paper was sponsored by the Atomic Energy Commission.

[2] Atomic Energy Commission Postdoctorate Research Fellow in the Physical Sciences of the National Research Council, 1949–50.

[3] Present address: Organic Chemistry Department, Imperial College of Science and Technology, London S. W. 7, England.

TABLE 1

SURVIVAL TIME OF MICE BEARING MYELOID LEUKEMIA C1498

Ref. No.	Formula and name	MLD/50 mg/20g mouse	Dose mg/20g mouse	No. IP injections weekly	Mean survival time (days)	Mean survival time of controls
1	2,4,6-Triamino pyrimidine sulfate 	> 40	4.0	3	10.8	10.3
2	4,6-Diamino-2-mercaptopyrimidine 	> 40	4.0	3	10.3	10.3
3	4,5,6-Triamino-2-mercaptopyrimidine sulfate 	40	4.0	3	8.0	10.3
4	2,4,5-Triamino-6-hydroxypyrimidine sulfate 	2.5	1.0	3	10.2	10.3
5	2-Amino-6-hydroxy-8-mercaptopurine 	0.5	0.2	3	10.5	9.5
6	2,6-Diamino-8-mercaptopurine 	1.0	0.6	3	5.0	9.5

versely affecting the whole animal. Hitchings (*3*) and Burchenal (*4*) have demonstrated the adenine inhibition of 2,6-diaminopurine, and Roblin (*5*) and Kidder (*6*) showed the antimetabolite action of 8-azaguanine.

In this laboratory we have been working on the synthesis of some thiazolinopurines related to 2,6-diaminopurine[4] and to other purines to be reported later. None of the compounds prepared in this program to date showed any cancer-inhibiting action, but they are being reported in an effort to avoid duplica-

[4] The syntheses of these compounds are being reported elsewhere.

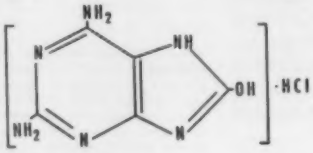
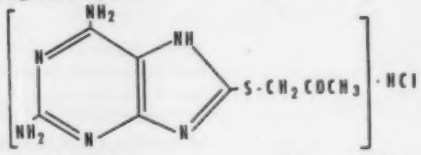
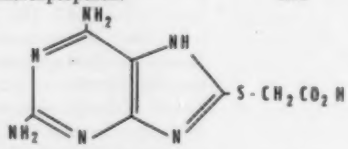
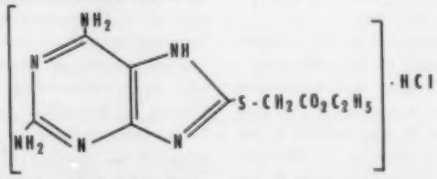
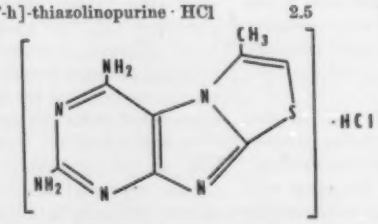
Ref. No.	Formula and name	MLD/50 mg/20g mouse	Dose mg/20g mouse	No. IP injections weekly	Mean survival time (days)	Mean survival time of controls
7	2,6-Diamino-8-hydroxypurine · HCl	5.0	0.4	3	4.0	7.5
						
8	2,6-Diamino-8-acetonylmercaptopurine · HCl	50	20	14	6.0	11.0
						
9	2,6-Diamino-8-carboxymethylmercaptopurine	0.05	0.02	3	9.0	9.5
						
10	2,6-Diamino-8-carbethoxymethylmercaptopurine · HCl	0.5	0.2	3	5.0	9.5
						
11	2,6-Diamino-4′-methyl-[3′,2′-h]-thiazolinopurine · HCl	2.5	1.0	3	9.8	10.3
						

TABLE 2

SURVIVAL TIME OF MICE BEARING MAMMARY TUMORS (Eo771)

5	2-Amino-6-hydroxy-8-mercaptopurine	0.5	0.2	3	8.0	22.5
6	2,6-Diamino-8-mercaptopurine	1.0	0.6	3	10.5	22.5
7	2,6-Diamino-8-hydroxypurine · HCl	5.0	0.4	3	23.0	22.5
8	2,6-Diamino-8-acetonylmercaptopurine · HCl	50	20	14	12.5	21.0
9	2,6-Diamino-8-carboxymethylmercaptopurine	0.05	0.02	3	19.5	22.5
10	2,6-Diamino-8-carbethoxymethylmercaptopurine · HCl	0.5	0.2	3	15.0	22.5

tion by other investigators. Some of the pyrimidines reported were used as intermediates in other syntheses, but they are included here since their antileukemic possibilities had not previously been explored.

The customary screening procedure was carried out using C57 black mice into which had been implanted

either the undifferentiated adenocarcinoma Eo771 or the myeloid leukemia C1498. Dosage of the compounds to be screened was arbitrarily set at 40% of the MLD/50 dose, except in cases where the animals reacted unfavorably to this amount.

Recently Skipper (*7*), working with Ak 4 mouse leukemia, reported that substitution of the 8-position of 2,6-diaminopurine eliminates its antileukemic activity. These results are confirmed by our data. Studies are now in progress with purine derivatives, similar to those in Table 1 (6–11), in the adenine, guanine, and isoguanine series.

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Utilization of C^{14}-labeled Glucose by Cardiac Muscle Treated with a Cardiac Glycoside

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Investigations in several laboratories have shown that cardiac muscle tissue exposed *in vitro* to a cardiac glycoside, or isolated following administration of the drug *in vivo*, respires at a markedly elevated rate (*1*). Because this increase in respiration is restricted to intact tissue and is a function of the concentration of appropriate exogenous substrate, it has been attributed to an increase in the rate of permeation of the substrate into the cell. This paper provides evidence that the phenomenon requires a different explanation.

Ouabain in a final concentration of 5×10^{-7} *M* was added simultaneously with C^{14}-labeled glucose to slices of dog myocardium respiring in substrate-free medium. The $C^{14}O_2$ evolved in the oxidation of the sugar was absorbed by the alkali in the center cup of the respirometer vessel. Table 1 shows that the stimulation of respiration by the cardiac glycoside was not accompanied by a greater uptake of glucose; on the contrary, somewhat less glucose was taken up than in the absence of the drug. However, the rate of glucose oxidation was doubled. According to calculations based on the data in Table 1, the fraction of glucose consumed which was oxidized to carbon dioxide and water rose from 16% to 38%. Comparison of the $Q_{C^{14}O_2}$ and Q_{CO_2}

[1] This work was supported by a grant from the Life Insurance Medical Research Fund. The author wishes to express his thanks to Robert E. Olson for a gift of glucose evenly labeled with carbon 14 and for his interest in the problem, and to Elizabeth White for measuring the radioactivity of the samples.

Table 1

Effect of Ouabain on the Utilization of C^{14}-labeled Glucose by Slices of Dog Ventricular Cardiac Muscle

Treatment	$Q_{glucose}$	$Q_{lactate}$	$Q_{keto\ acid}$	$Q_{C^{14}O_2}$	Q_{CO_2}	Q_{O_2}
Control	3.03	1.61	0.07	2.97	7.80	8.33
5×10^{-7} *M* Ouabain	2.69	0.63	0.02	6.08	11.07	11.18

~ 150 mg of slices (wet wt) per vessel, shaken in 2.85 ml modified Krebs-Ringer-phosphate solution (*4*); O_2 atmosphere, 38° C. Glucose (16.1 micromoles) and ouabain added after 45 min; 2-hr incubation period in glucose. All quantities are expressed as µl ideal gas (N.T.P.) absorbed or evolved /mg dry tissue/hr.

values shows that the acceleration of cardiac respiration by ouabain is quantitatively accounted for by the increase in the rate of glucose oxidation.

Table 1 indicates further that lactic acid production by cardiac slices during aerobic incubation in glucose is greatly reduced by ouabain. The $Q_{lactate}$ declined from 1.61 to 0.63. The change in keto acid production was minor in comparison. Since endogenous lactate formation was nil, one can calculate from the data that the amount of glucose consumed which was converted to lactate decreased from 28% to 11%. And, since the decrease in lactate appearance was not accompanied by synthesis of glycogen,[2] it is also evident that most of the extra glucose oxidized under the influence of ouabain would, in the absence of drug, have been glycolyzed.

Suppression of aerobic glycolysis by ouabain has also been observed in smooth muscle (*2*). In brain cortex, on the other hand, which is the only animal tissue besides heart muscle that has been found to respond to cardiac glycosides with an increase in respiration, these drugs strongly stimulate aerobic glycolysis (*3*). The greater abundance of the Krebs cycle phorase enzymes relative to the glycolytic enzymes in heart muscle as compared to brain cortex may be responsible for the difference in the metabolic response of these two tissues to cardiac glycosides.

It has previously been reported (*4*) that in the presence of pyruvate, which increases the rate of oxygen consumption of cardiac slices to the level attained following addition of a cardiac glycoside in glucose or in lactate, the drug causes no further increase in metabolism. One may infer that in cardiac muscle the cardiac glycosides accelerate the formation of pyruvate from glucose and lactate. Experiments aimed to test this hypothesis are now in progress in this laboratory.

Little can be said at this stage concerning the significance of the present findings with regard to the action of the cardiac glycosides on cardiac function. As has been pointed out before (*4*), it seems unlikely that the stimulation of cardiac energy metabolism by

[2] The glycogen content of the slices declined rapidly during the preliminary incubation and remained uniformly very low (about 20 mg/1,100 g) during the experimental period.

these compounds is the cause of the increase in the force of contraction or of other effects on the function of the myocardium. More probably, the functional and metabolic changes are both products of a cellular alteration the nature of which still remains to be disclosed.

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The Reduction of Triphenyltetrazolium Chloride by Dehydrogenases of Corn Embryos

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The fact that triphenyltetrazolium chloride is reduced to the red formazan by enzymes of viable tissue has been shown by several authors (*1–3*). Jerchel and Möhle (*4*) reported that the apparent redox potential (E'_0 at pH 7.0 of 2,3,5-triphenyltetrazolium chloride was about – 0.08 v. This fact suggested that the compound might be reduced through the catalytic action of certain pyridine nucleotide dehydrogenases, for the redox potentials of most of these enzyme systems fall below – 0.08 v. One of these systems, glucose dehydrogenase, was found to reduce the tetrazolium salt (*2*). Kun and Abood (*1*) reported that succinic dehydrogenase, which does not require a coenzyme, also reduced the tetrazolium compound at pH 7.4 and that the amount of formazan produced could be used as a measure of succinic dehydrogenase activity. The reduction by succinic dehydrogenase is unexpected, for the redox potential of the succinate/fumarate system is 0.00 v at pH 7.0. Fred and Knight (*5*) found that sodium malonate, sodium azide, 2,4-dinitrophenol, sodium fluoride, and iodoacetic acid at *M*/100 concentration merely slowed reduction of the salt by *Penicillium chrysogenum*. From this lack of specificity of inhibitors, the authors of the latter article concluded that a number of enzyme systems are able to reduce the dye.

We have investigated several enzyme systems, prepared from corn embryos, as to their ability to reduce the tetrazolium reagent. The apoenzyme mixture was prepared by the following method: Corn kernels were placed in water overnight, and the embryos were removed from the remainder of the kernel, extracted with acetone, dried, and ground with water. The extract was pressed out, centrifuged, and dialyzed. The solution was brought to pH 5.7, centrifuged, adjusted to pH 7.0, and saturated with ammonium sulfate. The precipitate was filtered, dried on a porous plate, and finally dried *in vacuo* over sulfuric acid. Diphosphopyridine nucleotide (DPN) was prepared by the method of Williamson and Green (*6*), and triphosphopyridine nucleotide (TPN) was prepared by the method of Adler, Elliot, and Elliot (*7*).

The ability of pyridine nucleotide enzyme systems to reduce the tetrazolium salt was determined by preparing solutions containing equal volumes of 1% apoenzyme preparation, 0.1% coenzyme, 0.5% tetrazolium salt, 4% substrate, and *M*/15 phosphate buffer (pH 6.6). The solutions were placed in the dark at room temperature and examined for color formation after 45 min.

TABLE 1

REDUCTION OF TRIPHENYLTETRAZOLIUM CHLORIDE BY CORN EMBRYO DEHYDROGENASES

Dehydrogenase System	Coenzyme	Substrate	Redox Potential at pH 7.0		Color Developed in 45 Min
Succinate/fumarate	....	Sodium succinate	0.00	Kalckar (1941)	None
Glutamate/α-ketoglutarate	DPN	Sodium glutamate	– 0.03	" "	"
Malate/oxalacetate	DPN	Sodium malate	– 0.102	Lehmann and Jorgensen (1939)	Pink
Ethyl alcohol/acetaldehyde	DPN	Ethyl alcohol	– 0.163	Kalckar (1941)	"
Lactate/pyruvate	DPN	Sodium lactate	– 0.18	Barron and Hastings (1934)	"
Glyceraldehyde-3-phosphate/1,3-diphosphoglycerate	DPN	*Sodium fructose diphosphate	– 0.28	Ochoa (1946)	"
β-Hydroxybutyrate/acetoacetate	DPN	Sodium-β-hydroxybutyrate	– 0.293	Hoff-Jørgensen (1938)	"
Isocitrate/oxalosuccinate	TPN	Sodium isocitrate	– 0.30	Ochoa (1946)	Pink (after 24 hr)
Glucose/gluconate	DPN	Glucose	– 0.45	" (1946)	Pink
α-Glycerophosphate/triosephosphate	DPN	Sodium-α-glycerophosphate			"

* Aldolase was assumed to be present.

The dehydrogenase systems shown in Table 1 were tested under aerobic conditions. Similar results were obtained when the solutions were placed in evacuated Thunberg tubes. When the enzyme system reduced the tetrazolium salt, the omission of enzyme, coenzyme, or substrate resulted in no color formation.

The following pyridine nucleotide dehydrogenases requiring DPN reduced the tetrazolium salt: glucose dehydrogenase, alcohol dehydrogenase, malic dehydro-

genase, β-hydroxybutyric dehydrogenase, lactic acid dehydrogenase, 3-phosphoglyceraldehyde dehydrogenase, and α-glycerophosphate dehydrogenase.

Triphenyltetrazolium chloride was also reduced by isocitric dehydrogenase, a pyridine nucleotide dehydrogenase requiring TPN, but the reduction was very slow as compared to the DPN enzyme systems.[1]

When sodium glutamate was employed as the substrate, no color developed, although glutamic dehydrogenase has been shown to be present in seeds (*8*). Since the redox potential of this dehydrogenase system has been reported as −0.03 v, it is possible that the enzyme, even though present, would not reduce the tetrazolium salt.

The addition of sodium succinate to the enzyme mixture prepared from corn embryos did not result in the reduction of the tetrazolium salt at pH 6.6. At this pH the redox potential of the succinate/fumarate system probably is above the redox potential of the tetrazolium salt, and a reaction should not be expected. However, the addition of coenzyme and sodium succinate to the enzyme preparation resulted in a reduction of the salt. Possibly this indicates that succinic dehydrogenase was present in the enzyme mixture and that the reduction of the tetrazolium salt only took place through the action of pyridine nucleotide systems which were one or more steps removed from the succinate reaction.

[1] The dimethyl ester of isocitric lactone was kindly supplied by H. B. Vickery, of the Connecticut Agricultural Experiment Station.

It is probable that the reduction of triphenyltetrazolium chloride by viable corn embryos can take place if one or more dehydrogenase systems with favorable redox potentials are present. The presence of active enzyme systems does not necessarily indicate seed viability, but the absence of active dehydrogenases probably indicates loss of germinating ability.

Because of the simplicity of the equipment and procedure, the elimination of the use of flavoprotein and cytochrome preparations, and the stability of the formazan, the use of triphenyltetrazolium chloride provides a convenient method for determining the presence of certain dehydrogenases.

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Comments and Communications

Paper Ionophoresis

In a recent communication by McDonald, Urbin, and Williamson (*Science*, **112**, 227 [1950]), and experimental technique was described for the separation of various ions on filter paper strips saturated with electrolyte solutions across which an electric potential had been impressed. They also used this same method to determine mobilities of certain ions. It is certainly true that this method is, in many cases, capable of giving good ionic separations, as these authors have concluded. However, it is open to question whether the experimental conditions reported are satisfactory for determination of ion mobilities.

In a recent publication (*J. Am. Chem. Soc.*, **72**, 2943 [1950]) we pointed out that the progression of certain ions along filter paper under conditions essentially similar to those described by McDonald *et al.* was not a linear function of time. Although it is true that our experimental conditions were not exactly the same as those reported by McDonald *et al.*, all the essential elements upon which the following discussion bears were present in both studies. That is to say, electrolyte was fed continuously to the filter paper by capillary forces from both its ends, which were immersed in electrolyte supply vessels during the time a current flowed through the paper; the paper hung free in a surrounding enclosed vapor space; and the mixture to be separated was applied to the paper at an intermediate point.

It is manifest that, for any method to be suitable for ion mobility studies, the following minimum conditions be met:

1. Adsorption must not be a factor, or must be corrected for if present.
2. Electroendosmosis must be taken into account in cases where appreciable zeta potentials are to be anticipated.
3. The path through which the ion migration is observed must be uniform with respect to the applied electrical field, with respect to its ionic composition, and with respect to temperature.

None of these factors apparently has been given consideration in the paper under discussion.

With respect to point 1, it is conceded that some ions behave on paper saturated with electrolyte solutions in a manner similar to their behavior in "free solution." However, this factor is strictly dependent upon the system under consideration and, in certain instances in our own experience (e.g., with the dye acridine orange in certain electrolytes), strong adsorption may altogether preclude the application of this technique.

With respect to point 2, the authors make the statement that electroendosmotic flow did not appear to be

a serious effect. However, they base this conclusion upon the fact that their experimental values happen to agree (within 17% in the case of nickel in nickel sulfate) with values obtained by the conventional Hittorf method. In our own experience at pH's far removed from pH 2, electroendosmosis may require a correction factor of as much as 20% (see above-mentioned reference, paragraphs dealing with apparent cathodic migration of gamma globulin at pH 8.6). However, even in a system in which adsorption between the ion to be measured and the filter paper does not occur, and in which correction is made for the electroendosmotic flow, it is probable that insurmountable difficulties would exist under the experimental conditions reported.

When currents of the order reported (1–3 ma) are caused to flow through narrow strips of filter paper that have been saturated with most electrolytes, appreciable heat is developed in the strip. As a result, water distills from the paper. (We have checked this point using the conditions reported—i.e., with E. & D. No. 613 paper strips 1 and 2 cm wide saturated with 0.1 N · KCl. When currents even as low as 1 ma were caused to flow through the paper, gross distillation from the paper, with condensation on the enclosing vessel, was observed.)

Since the paper is dried by this procedure and its state of capillary saturation is decreased, capillary forces continuously "siphon" fresh electrolyte from the buffer vessels into the paper. The fact that the electrolyte solute used is not volatile adds further complications. As a result of the above distillation, the KCl concentration is being continuously increased on the paper during the course of the experiment. This is not, of course, a linear function along the path of ion migration.

Each succeeding increment of filter paper beyond the buffer vessel receives less volume of electrolyte by the amount that has been evaporated in the preceding increment. Since the actual cross section of the paper is constant, a *flow rate gradient* results in the fluid flow along the length of the filter paper strip from each buffer vessel, decreasing as the center of the paper is approached. (Electroendosmosis augments this flow rate on the anode side of the center and diminishes this flow rate on the cathode side.) Then, in analogy, the ions applied at the center of the paper must "swim" upstream against a current that is constantly increasing in swiftness as the electrode vessels are approached. In fact, this effect is so definite that we have been able to design experiments (in press) in which ions falling within certain ranges of mobility actually reach stationary positions of mobility equilibrium where their tendency to flow upstream in consequence of their charge in the electric field is exactly counterbalanced by the countercurrent flow of electrolyte toward the center of the paper. Furthermore, these final equilibrium positions are quite *independent of the point of application* of the particular ion to the paper.

The complications resulting from the progressive increases in concentration of solute in cases of nonvolatile solutes could be avoided theoretically by utilizing as electrolyte a volatile solute which forms, with water, an azeotrope of constant composition, and by utilizing this particular mixture as electrolyte so that, when distillational equilibrium was achieved, a constant ionic strength would be maintained on the paper. However, this would not eliminate the flow gradients that we have observed.

In our own experience, temperature control of the strip is very difficult to achieve under the conditions reported by McDonald *et al.*, except in cases where very low currents are permitted to flow, since cooling, limited to the processes of convection and radiation, does not seem to be adequate under these conditions to dissipate the heat produced.

We have found that, if the vapor space surrounding the strip is eliminated, temperature control is simplified by permitting the process of conduction to be used for cooling. At the same time, the distillational equilibria and accompanying fluid flow gradient can be eliminated. This can be carried out in a number of ways, perhaps most conveniently by clamping the paper strip between plate glass strips (preferably treated with an antiwetting agent—for example, one of the silicone preparations). "Edge effects" can be reduced by limiting observations to migration near the center axis of relatively wide strips or, in the case of narrow strips, by utilizing gaskets which are placed at the edges of the paper strip, and which are conveniently made of the filter paper under investigation, saturated with a silicone grease to define an enclosed channel completely filled by the filter paper strip. Another satisfactory method is to place the paper in carefully fitted shallow channels machined in lucite blocks that are provided with carefully fitted covers.

Where currents are high and heating must be eliminated, we have found that it is satisfactory to place the strips on aluminum blocks partially immersed in equilibrium ice baths, a thin layer of electrical insulation being placed between the paper strip and the metal. (G. W. Smith and K. A. Kraus have independently used a similar method for this purpose [personal communication].)

An ingenious method of correcting these difficulties has been suggested by A. Tiselius (personal communication), wherein the paper strips saturated with electrolyte solution are immersed in water-immiscible, nonpolar liquids to provide a seal about the paper and a medium for removing by conduction any heat developed. The latter method would presumably be suitable for systems in which the components to be separated do not possess large nonpolar constituent groups that might interact with the nonpolar sealing and cooling medium at the polar-nonpolar interface. (In certain polar-nonpolar systems we have experimental evidence, however, that this interaction at the interface may lead to "chromatographic" separation in the absence of any electrical potential.)

In view of the above considerations, it seems probable that it is only fortuitous that the results reported by McDonald *et al.* approach the Hittorf values as closely as they appear to.

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On a Recent Proposal to Correct an Error Committed by the International Commission on Zoological Nomenclature at the Paris 1948 Meeting

On October 28, 1950, Francis Hemming, Secretary to the International Commission on Zoological Nomenclature, undertook to circularize by mail the taxonomists working on the insect order Lepidoptera to determine their views on a proposition to correct a serious error made by the commission in its haste at Paris in 1948. Several important principles are involved in this proposal, with implications far beyond the name of the Monarch Butterfly, which was directly involved.

In brief, the proposal is a further extension of Mr. Hemming's campaign to replace the Law of Priority with *Nomina Conservanda*. Like so many previous cases, his proposal is accompanied by almost no justification beyond the statement that "greater confusion than uniformity" would result. His direct statements that "the name universally applied to" the Monarch is *plexippus* and that the Indo-Oriental species involved "is now universally known as *Danaus genutia*" are not only in error but are not even close to the truth.

Furthermore, Mr. Hemming proposes to take no account whatever of a careful lectotype designation already published; he proposes to designate a published illustration as a type of a species; and he proposes to designate a new type locality for that species which is not even the locality of the figured specimen. In choosing this figure, in a group of animals where color is of great importance in taxonomy, he chooses a black-and-white figure, stating that no colored figure is available. At least 4 of the best-known works on American butterflies, from 1904 to 1948 in at least 18 editions, have colored figures that could have been used.

In circulating his proposal Hemming neglected to send a copy to several prominent interested lepidopterists, including the author of the only modern revision of the subfamily involved. (We note with interest that this man had previously taken a stand opposite to that now taken by Hemming.)

These principles and the method of action proposed by Hemming are so objectionable to us that we feel it necessary to present our criticisms and suggestions. We believe that many taxonomists working in other groups will be equally interested in the case.

At the 13th meeting of the International Commission at Paris in 1948, it was the intention of the commission to fix the trivial name *plexippus* Linnaeus, 1758, to the North American species known as the Monarch Butterfly. Linnaeus had proposed *plexippus* for specimens collected by Peter Kalm in North America and for his own specimens from China, and the name had since been applied to the 2 separate and distinct species found in these two regions. But lepidopterists were not agreed as to whether there was a type for *plexippus*, and the application of the name was thus a matter of opinion. The commission attempted to carry out their intention by designating an official figure (Holland. *Butterfly Book*, pl. 7, Fig. 1, [1931]) to replace the type. They erred in carelessly assuming that this represents the North American Monarch, for it actually is a figure of a distinct subspecies of that butterfly occurring in northern South America and parts of Central America. Thus the name *Danaus plexippus plexippus* (L.), 1758, was fixed to the South American subspecies, and the name of the North American subspecies became *Danaus plexippus menippe* (Hübner), 1816. Hence, the Commission's hurried action resulted in quite a different fixation than that intended. This error has already been discussed by one of the present writers (Field. *Proc. Entomol. Soc. Wash.*, 52, 234 [Oct. 1950]).

Hemming's proposal would correct this error by deleting from the Opinion to be rendered the reference to Holland's figure and substituting a reference to another figure in its place (Clark. *Proc. U. S. Nat. Museum*, 90, pl. 71, Fig. 1 [1941]) and further by designating a type locality, "Pennsylvania."

We are strongly against this proposal for three reasons.

First, because we believe that a strict application of the Law of Priority will serve the best interests of all concerned. Linnaeus' own material came from China and represented the Indo-Oriental species (sometimes referred to as *genutia* Cramer). We know this because he definitely states (in *Mus. Lud. Ulr.*, 262 [1764]) *"meus e China."* It is clear that Linnaeus confused several species under the name *plexippus*, for although 2 of the 4 literature references listed by Linnaeus in his original description (*Systema Naturae*, Ed. X, 471 [1758]) refer to the North American Monarch, the other 2 refer to still another distinct New World species. The first part of the Linnaean description would fit either of these American species or the Indo-Oriental species, but he added at the end of his description a sentence (*"alæ primores fascia alba, ut in sequente"* [*chrysippus*] *"cui similis"*) that could apply only to the Indo-Oriental species. The fact of the matter is that Linnaeus intended the name for the Indo-Oriental species (his Chinese specimens) and at the same time misidentified these American species with this Indo-Oriental species.

Corbet (*Proc. Roy. Entomol. Soc. Lond.*, 18, pts. 9–10, 188 [Oct. 1949]) has already presented a perfect case for applying the name to the Indo-Oriental species and has designated a Chinese specimen in the Linnaean Collection in London as the lectotype, for he says, "I have no hesitation in taking the male specimen bearing the Linnaean name label" (in Linnaeus'

handwriting) "as the name-type of *P. plexippus*." We regard this an an unequivocal designation of a lectotype.[1] By accepting Corbet's action as final we would be following the intent of Linnaeus.

Second, we are opposed to this proposal because we believe the evidence advanced by Hemming and Corbet to support a *nomen conservandum*[2] is not conclusive.

It is claimed that the application of the name *Papilio D. plexippus* Linnaeus, 1758, to the Indo-Oriental species would result in greater confusion than uniformity. Hemming, in presenting the proposal to place this name on the Official List of Specific Trivial Names in Zoology and to conserve it for the North American species, states that it would be most confusing to apply the trivial name *plexippus* to a species other than the North American Monarch.[3] Further, on page 2 under point (7) of the present proposal sent out to specialists by Mr. Hemming, he states that "Dr. Corbet realized the confusion to which this conclusion would give rise." On page 2 under point (4) he says: ". . . this species" (the North American one) "came to be known as *Danaus plexippus* (Linnæus), the name universally applied to it."

We believe that these statements cannot be justified by the facts. We ask, Confusing to whom? Universally applied to it by whom? The American species is not now, and never was, universally known as *plexippus*. If we examine the record (figures compiled from the revision of the American Danaidae by D'Almeida. *Mem. inst. Oswaldo Cruz*, **34**, fasc. 1, 44 [1939]), the following is evident. Six different names have been applied to the North American Monarch. The name most commonly used is *archippus* in slightly over 49 per cent of the literature (individual references), whereas the name *plexippus* has been used in only about 30 per cent of the literature on the North American species. After Barnes and Benjamin (*Can. Entomol.*, **56**, 16 [1924]), pointed out that *archippus* was a homonym and that *Danaus menippe* (Hbn.) should be used for the North American species, the name *archippus* gradually dropped out of the literature and was replaced by the names *plexippus* and *menippe*. D'Almeida (see above) rejects the name *plexippus* for the North American species and applies it to the Indo-Oriental species. Forbes uses the name *menippe* for the North American species in 1939 (*J. N. Y. Entomol. Soc.*, **51**, 297). Talbot, in his paper "Revisional Notes on the Genus *Danaus Kluk*" (*Trans. Roy Entomol. Soc. Lond.*, **93**, pt. 1, 115 [1943]), uses the name *menippe* for the North American species and the name *plexippus* for the Indo-Oriental one. Not only Talbot, Forbes, Barnes, and Benjamin, but a number of others, have used the name *menippe* for the North American species, so that there are altogether approximately 20 separate papers in which the name *menippe* is used for the North American species.

Hemming further states (on p. 2, under point (5) of the proposal being here discussed) that ". . . Species 'B'" (the Indo-Oriental species) ". . . is now universally known as *Danaus genutia* (Cramer)." We believe that this also is a misstatement of fact. According to the latest catalogue treating the literature for the Indo-Oriental species (Bryk. *Lepidopterorum Catalogus*, pars 78, Danaidae I, [1937]), there are 64 references in which the Indo-Oriental species (the typical subspecies, plus its forms) is treated as *plexippus* and about 30 in which it is treated as *genutia*. In other words, there are twice as many references in which the name *plexippus* is used for the Indo-Oriental species as there are references in which the name *genutia* is used for this species. If we consider the literature for all the subspecies of the Indo-Oriental species, it is immediately apparent that there is an overwhelming preponderance of usage for the name *plexippus* as opposed to *genutia*. Even in the total usage for the name *plexippus* in literature, we see that this name has been used in 64 references of the Indo-Oriental species and only slightly more often (68) in references to the American insect.

In a survey made of the usage of the names *plexippus*, *genutia*, *menippe*, and *archippus* by Talbot (*Trans. Roy. Entomol. Soc. Lond.*, **93**, pt. 1, 115 [1943]) made from books written by reputable authors in systematic and faunistic work, he stated that a large majority of those who recorded the Indo-Oriental species used the name *plexippus* for that species, whereas most of those who recorded the American insect did not use the name *plexippus* but used the name *archippus*.

In the face of these facts, how can it be claimed that there would be more confusion than uniformity in applying the name *plexippus* to the Indo-Oriental species?

Our third objection to this proposal is our belief that the method to be employed to fix this name to the American species is contrary to the best modern nomenclatural practices and is, indeed, somewhat contradictory. It would be equally objectionable to use this method to fix the name to the Indo-Oriental species.

We object to the designation of a published picture to represent a type, when there are still specimens available in the original collection from which to choose a type, and especially when one of these original specimens has already been selected as a lectotype! In the last analysis (when original specimens are available), the only true and correct method of identifying a name is to resort to an official (type) specimen that represents that name. Modern systematics of Lepidoptera often requires that structures not ob-

[1] Before taking any action in this case the commission should first consider this designation. Corbet's designation should be voided before any attempt is made to apply the name *plexippus* to the North American species.

[2] The International Congress of Zoology, meeting in Monaco in 1913, gave the International Commission on Zoological Nomenclature the plenary power to suspend the rules where in its (the commission's) judgment the strict application of the rules would clearly result in greater confusion than uniformity.

[3] It is our belief that it might perhaps be inconvenient, but no more confusing one way than the other.

servable in pictures be studied in order to identify species. Very often type specimens have to be dissected and studied in minute detail to settle questions of identification. In such cases official figures would be of no use. Why continue to foster a practice that very possibly someday would be of no aid in settling questions of identification, a practice that very likely would still have to be further clarified?

In addition to the objection above to the designation of published type figures instead of type specimens, we most certainly object to the designation of an official figure made from a specimen collected from one locality and the designation of another locality as the type locality. In this case Hemming would delete from the Opinion to be rendered, the reference to the Holland figure and substitute as the official figure one published by Clark (*Proc. U. S. Nat. Museum*, **90**, pl. 71, Fig. 1),[4] a figure that was made from a specimen collected by H. S. Burnett at Kendall, New York. Hemming, then, would further designate as the type locality "Pennsylvania." Does not this action have the effect of making, in a backhanded fashion, the specimen illustrated by Clark a sort of type for the species, if not an actual type? The locality in which this specimen was collected would become another type locality, and thus we would have two type localities. What could be more confusing?

We further submit that, if it is decided to designate an American locality as a type locality, something more definite could be selected than Pennsylvania, for Peter Kalm (the collector of the American material studied by Linnaeus) has given us an excellent account of his travels in America (for the latest account of his travels in English, see A. B. Benson, *Peter Kalm's Travels in North America*, 2 vols. New York: Wilson-Erickson [1937]). It can be determined from this work that his explorations extended from the state of Pennsylvania to New York, New Jersey, and southern Canada. All localities where Kalm spent some time are mentioned by name, and in addition dates are given. Much time was spent around Philadelphia, so that this could be designated as the type locality, and this would certainly be more useful and specific as a type locality than "Pennsylvania." On the other hand, a good case could be presented for Fort St. Frédéric (Crown Point), New York, being the locality where Kalm may have collected the North American Monarch, for in his account of this locality (see work by Benson mentioned above, 387, 574) he mentions the abundance of *Asclepias syriaca* and *Asclepias variegata*, two of the food plants of the Monarch.

Because of the objections to the present Hemming proposal presented above, we request that the commission reconsider the whole matter of fixing the name *Papilio D. plexippus* L., 1758; we further express the hope that the commission (instead of suspending its rules of procedure as it did at Paris—see *Bull. Zool. Nomen.*, **4**, pts. 1–3, 7, [1950]) will follow the rules of procedure agreed to and adopted at the third session in Paris, 1948 (*ibid.*, 55). These rules would require the publication of a notice of a proposal to suspend the rules in the *Bulletin of Zoological Nomenclature* and in two other serials, *Nature* (published in Europe) and SCIENCE (published in America). These rules would give specialists, institutions, laboratories, and all interested persons a six-month period[5] to present arguments for or against the suspension under consideration and would require at least a two-thirds majority of the commission voting on the proposition in order to suspend the rules.

In closing, we should like to add that it is regrettable that Secretary Hemming failed to send copies of his proposal to all prominent specialists in Lepidoptera (we know of 6 who did not receive this proposal by this date, December 10, 1950).[6] Furthermore, no space was provided for a record of the names of interested specialists who disagreed with his proposal even though there was provided as point 7, page 6, of this proposal, a place for the names of specialists who thought the Hemming proposal would constitute the most satisfactory solution of the problem.

WILLIAM D. FIELD
J. F. GATES CLARKE
J. G. FRANCLEMONT

Washington, D. C.

[4] This figure of Clark's is a *black-and-white* half-tone and was apparently selected on the belief as stated by Hemming, that "There is in fact no coloured figure" of the North American subspecies "to which reference can be made, . . ." This belief is, of course, absolutely false, as every student of American butterflies can verify. We cite four easily available references: Comstock, J. H., and Comstock, A. B. *How to Know the Butterflies*, pl. 32, Fig. 3, (1904, 1920, 1929); Lutz, F. E. *Fieldbook of Insects*, pl. 21, Fig. at top of pl. (1918, with twelve printings down to 1948); Comstock, J. A. *Butterflies of California*, pl. 17, Figs. 1, 2 (1927); Wright, W. G. *Butterflies of the West Coast*, pl. 12, Fig. 100 (1905).

[5] We would prefer the one-year period originally required by the International Congress of Zoology, meeting in Monaco in 1913.

[6] It is most interesting to note that one of these six men is R. Ferreira d'Almeida (of the staff of the National Museum of Brazil), the author of the only modern and complete revision of the subfamily Danainae of the New World (*Mem. inst. Oswaldo Cruz*. **34**, fasc. 1, pp. 1–113, 30 pl. [1939]).

News and Notes

Veterans Administration Radioisotope Conference

George M. Lyon

Radioisotope Section, Research and Education Service, Department of Medicine and Surgery, Veterans Administration

THE FIFTH SEMIANNUAL CONFERENCE of the directors of the radioisotope program of the 14 Veterans Administration hospitals with radioisotope laboratories was held in the hospital at Framingham, Mass., on November 29–December 1. Problems in the use of radioiodine in studying function and disease of the thyroid gland occupied the first day and a half of the session. The second day and a half were devoted to training programs being conducted for Veterans Administration personnel in three different but closely related fields of interest: "The Medical Aspects of Atomic Warfare," "The Medical Aspects of Radiological Defense," and "Radiological Defense (Monitors)."

Herbert Allen and Raymond Libby, of the Los Angeles hospital, described the successful use of 1 microcurie of radioiodine in evaluating thyroid function. This has been made possible by the employment of a scintillation counter developed by Benjamin Cassen and associates, of the Atomic Energy Project and the Medical School of the University of California at Los Angeles. Mortimer Morton, of the Long Beach hospital, described the successful use of a bismuth-walled Geiger-Mueller tube for a similar purpose when employing tracer doses of radioiodine varying from 0.2 to 10 microcuries. George LeRoy, of the Hines hospital, reported the successful use of 10 microcuries of radioiodine. Because of the advantages offered in the use of very small tracer doses of radioiodine for clinical diagnostic purposes, a considerable effort was made during the past year to develop techniques aimed at the use of 10 microcuries of radioiodine or less. The use of 1 microcurie will permit repeated tests with complete safety as well as use of radioiodine in studying thyroid function in small children. Joseph Ross and others reported improvements in the use of radioiodine in a more accurate assessment of thyroid function.

During October and November, 373 Veterans Administration personnel, other than physicians and nurses, received basic instruction in "Radiological Defense." These will constitute the "monitors" for 123 radiological defense teams for Veterans Administration hospitals. In evaluating the training activities, 80 hours of combined formal and practical instruction were considered the minimum time requirement for basic instruction. A continuing in-service training program will include monthly or semimonthly practice periods.

Instruction for physicians of the Veterans Administration in the "Medical Aspects of Atomic Warfare" has been given in several of the hospitals having radioisotope programs. Ten hours of formal instruction have proved to be adequate for this purpose.

Basic instruction for selected physicians of the Veterans Administration in the "Medical Aspects of Radiological Defense" is planned for implementation early this year. It is considered that 30 hours of combined formal and practical instruction will be required for this purpose. It will be possible to permit practical exercises in conjunction with the radiological defense teams in the hospital where the training is conducted.

This training program has been made possible because of the existence of qualified personnel, equipment, and facilities employed in the peacetime application of atomic energy in the radioisotope laboratories of the 14 Veterans Administration hospitals having radioisotope units, and may be considered as a worth-while contribution of such a program. In 7 of the hospitals, serving either on a full-time basis or as consultant-instructors, were individuals who had practical experience in radiological safety operations in one or more atomic bomb tests.

Scientists in the News

Thomas D. Rowe has resigned as dean of the Rutgers University College of Pharmacy to become dean of the College of Pharmacy at the University of Michigan. Dr. Rowe has been chairman of National Pharmacy Week for the American Pharmaceutical Association since 1947. He will take up his new post on June 30.

The suit brought by **Albert Schatz,** Brooklyn College professor, against **Selman A. Waksman,** Rutgers University microbiologist, and the Rutgers Research and Endowment Foundation was settled late last month. Dr. Schatz retracted his charge that Dr. Waksman had used "fraud and duress" to induce him to assign to the foundation his rights in the patent on the drug streptomycin. For his part in the discovery of streptomycin, Dr. Schatz will receive 3 per cent of the net royalties from the drug starting October 1, 1950. He will also receive $125,000 for assignment by him of his rights in Canadian, New Zealand, Japanese, and all other foreign patent rights to the foundation. Dr. Schatz, a former student of Dr. Waksman, had

originally sought 50 per cent of all royalties for his part in the discovery. Dr. Schatz is one of 26 persons who worked with Dr. Waksman on the discovery and development of streptomycin who will receive financial recognition for their work. Net royalties to September 30, 1950, were approximately $2,360,000. Eighty per cent of the royalties will remain in the foundation, for further scientific research, including the work of the Institute of Microbiology.

Recent visitors at the Communicable Disease Center, USPHS, Atlanta, were **Akira Tanaka,** Public Sanitation Bureau, Welfare Ministry, Tokyo; **Luis Morato Proenca,** State Health Department, São Paulo; and **Erkki Klemola,** City Hospital for Communicable Diseases, Helsinki.

C. Richard Walmer, a senior fellow at the Mellon Institute of Industrial Research since 1946, has been named director of the Industrial Hygiene Foundation. He has been medical director of the foundation, which operates under the auspices of the institute, for four years. Dr. Walmer succeeds the late **John F. McMahon.**

Hideki Yukawa, winner of the 1949 Nobel prize in physics, will become professor of physics at Columbia University on July 1. He has been visiting professor at the university on leave from Kyoto University since 1949. Dr. Yukawa will teach advanced physics and will continue his research.

Meetings and Elections

The recently elected officers of the **Central States Section of the Botanical Society of America** are: chairman, G. W. Prescott, Michigan State College; vice chairman, Oswald Tippo, University of Illinois; secretary-treasurer, Robert L. Hulbary, State University of Iowa; member of the Executive Committee (three-year term), R. E. Cleland, Indiana University.

The First National Congress of Applied Mechanics will be held on June 11–16, at Illinois Institute of Technology, Chicago. The general chairman of the congress is L. H. Donnell, of Illinois Institute of Technology. Papers for presentation at the congress must be submitted before *April 14,* and should constitute original research in applied mechanics, which includes kinematics, dynamics, vibrations, waves, mechanical properties of materials and failure, stress analysis elasticity, plasticity, fluid mechanics, and thermodynamics. Papers should not be longer than 5,000 words. They will be grouped by subject, and half an hour will be allotted for presentation and discussion of each paper.

The 1951 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy will be held at the William Penn Hotel, Pittsburgh, Pa., March 5–7. The conference is sponsored by the Analytical Chemical Society and the Spectroscopy Society of Pittsburgh. An exposition of modern laboratory equipment will be a feature of the conference.

The American Academy of Forensic Sciences will hold its annual meeting March 1–3, at the Drake Hotel, Chicago. Persons desiring to present papers should write to A. W. Freireich, Chairman Program Committee, 180 Hempstead Ave., Malverne, N. Y. For additional information write to the office of the president, R. B. H. Gradwohl, 3514 Lucas Ave., St. Louis 3, Mo.

The AIBS Advisory Committee on Physiology for the **Office of Naval Research** met on December 2 to evaluate research proposals submitted during the past six months. Proposals for basic research in the various areas of physiology are now being accepted for consideration at the next meeting of the Committee, in Cleveland, May 4–5. The deadline for the reception of proposals is *March 15.* For further information address: Chief of Naval Research, Office of Naval Research, Department of the Navy, Washington 25, D. C. Attention: Physiology Branch, Code 441.

At the annual meeting of the **Association for Research in Nervous and Mental Disease** held December 15–16, the following officers were elected for 1951: president, S. Bernard Wortis; first vice president, John C. Whitehorn; second vice president, J. Lawrence Pool; secretary-treasurer, Clarence C. Hare; assistant secretary, Rollo J. Masselink.

The following is a schedule of the 1951 meetings of the **American Meteorological Society:** 109th national meeting, January 29–February 1, Hotel New Yorker, New York; 110th national meeting, May 2–3, Washington, D. C.; 111th national meeting, June 19–21, Los Angeles; and the 112th national meeting, October 9–11, Minneapolis.

The Institute of Medicine of Chicago announces the following officers for 1951: president, Walter H. Theobald; vice president, Charles W. Freeman; secretary, George H. Coleman; treasurer, E. Lee Strohl. Henry T. Ricketts has been reelected chairman of the Board of Governors.

The **National Bureau of Standards** will celebrate its 50th anniversary this year. Many of the principal scientific and technical organizations of the nation have planned meetings in Washington to honor the semicentennial. The meeting of the American Society of Photogrammetry (January 10–12) and the joint AIEE, IRE, NBS Conference on High Frequency Measurements (January 10–12) have already been held. Coming meetings are:

American Crystallographic Association, February 15–17
Inter-Society Color Council, February 28
Optical Society of America, February 28–March 3
Electrochemical Society, April 8–12
Union Radio Scientifique Internationale, April 16–18

National Academy of Sciences, April 23–25
APS Division of High Polymer Physics, April 26–28
American Physical Society. April 26–28
Bone Char Conference II, May 3–4
Acoustical Society of America, May 10–12
Horological Institute of America, May 14–15
Society for Experimental Stress Analysis, May 16–18
National Conference on Weights and Measures, May 22–25
Analytical Division, American Chemical Society, June 14–16
American Astronomical Society, June 21–23
Illuminating Engineering Society, August 26–September 1
International Union of Chemistry, September 13–15
American Roentgen Ray Society, September 25–28
American Dental Association, October 15–20
National Institute of Governmental Purchasing, October 21–24
Institute of Mathematical Statistics, October 26–27
American Mathematical Society, October 27
Conference on Electrical Insulation (NRC), October 29–31
APS Division of Electron Physics, November 1–3

In addition, a number of committee conferences and meetings of local sections of societies will be held at the bureau. The bureau is also planning a series of symposia on special topics.

Grants and Awards

The **John Fritz Medal** has been awarded to Vannevar Bush, president of the Carnegie Institution. Awarded jointly by the American Institute of Electrical Engineers, the American Society of Civil Engineers, the American Institute of Mining and Metallurgical Engineers, and the American Society of Mechanical Engineers, the medal will be presented during the annual winter general meeting of the AIEE at the Hotel Statler, New York, January 22–26.

Lists of foreign scholars who have been awarded **Fulbright travel grants** for lecturing or advanced research in the U. S. for the current academic year are available from the Committee on International Exchange of Persons, Conference Board of Associated Research Councils, 2101 Constitution Ave., Washington 25, D. C. Lists have been made for the physical, biological, and social sciences, and for education and the humanities, including for each scholar the date of arrival, length of stay, and the institution sponsoring the visit. It is the hope of the committee that universities and research institutions will invite visiting scientists to inspect their facilities and take part in scientific programs. Many visitors under the Fulbright program are leading research workers in their fields and can offer expert advice in return for the opportunity of becoming acquainted with American institutions of higher learning.

Establishment of an annual $1,000 award for outstanding contributions to chemical education, sponsored by the **Scientific Apparatus Makers Association,** Chicago, and administered by the American Chemical Society, has been announced. The activities recognized by the award may lie in the fields of teaching, organization and administration, influential writing, educational research, the methodology of instruction, establishment of standards of instruction, and public enlightenment.

Karl T. Compton, chairman of the Corporation of MIT, received the first award of the $1,000 **William Procter Prize for Scientific Achievement,** administered by the Scientific Research Society of America. It was given in recognition of Dr. Compton's record in scientific research, for his administration as president of MIT from 1930 to 1948, and for his work as chairman of many national committees concerned with research. The presentation was made December 29 at the AAAS meeting in Cleveland.

Lute J. Parkinson, mining consultant, was presented with the **Colorado School of Mines Distinguished Achievement Award** December 15. Given to graduates who make outstanding records in the mineral industries field, and who bring credit to themselves and the school, his was the 59th award made. He is a mining consultant for the Anglo-Chilean Nitrate Corporation and the Lautaro Nitrate Co., Ltd., of Antofagasta, Chile.

A gift of $5,250,000 from the **Alfred P. Sloan Foundation** will enable MIT to establish a new School of Industrial Management. The school will offer future industrial executives a correlated program in industrial problems as well as in science, engineering, and research. It will open in 1952.

Fellowships

Candidates are now being sought for the $2,500 **Merck Graduate Fellowship in Analytical Chemistry** sponsored by Merck & Co., Inc., Rahway, N. J., and administered by the American Chemical Society. The place of study must be an institution whose undergraduate course in chemistry is approved by the ACS; in Canada the institution must be approved by the Chemical Institute of Canada. A student is eligible to have the fellowship renewed twice, but no student may hold it for more than three years. Application blanks may be obtained from the American Chemical Society, 1155 16th St., N.W., Washington 6, D. C. They must be returned with letters of recommendation and transcripts of credits by *February 15.*

The Florida State University has announced the availability of graduate assistantships for study in meteorology and climatology. Appointments will be made in connection with research being conducted for ONR and the Air Materiel Command. The student will be excused from payment of the out-of-state tuition fee and permitted to carry as many as 10 hours of course work. Minimum requirement is a bachelor's

degree from an accredited institution, with two years of university mathematics and one year of university physics. Applications should be filed before *May 1*. Forms and information may be obtained from the Dean, Graduate School, The Florida State University, Tallahassee.

NRC News

Reports of recent research progress prepared by two committees of the **NRC Division of Geology and Geography** are available from the division office: *Report of the Committee on the Measurement of Geologic Time, 1949–1950* (118 pp., $1.00), and *Report of the Committee on a Treatise on Marine Ecology and Paleoecology, 1949–1950* (59 pp., $1.00). The geologic time report surveys recent work in the determination of isotope ratios, the chemical composition of certain minerals, the accurate measurement of feeble radioactivity, and similar research bearing on the problem of dating rocks and other natural materials. Several progress reports containing unpublished material submitted to the committee are included, and also some recent theoretical calculations on the time of formation of the elements by J. M. Lopez de Azcona, Instituto Nacional de Geofísica, Madrid. The report contains an annotated bibliography of recent articles related to the measurement of geologic time. The marine ecology and paleoecology report contains also the review of current research in the field and the bibliography of recent publication. Special sections include a complete annotated bibliography on the ecology of marine bacteria, and a discussion of the strontium cycle in the study of ecosystems.

Section III, *Reactor Engineering*, of NRC's *Glossary of Terms in Nuclear Science and Technology*, is now available in preliminary edition from the publishers, the American Society of Mechanical Engineers, 29 W. 39th St., New York 18. This is the third of nine proposed sections to be issued for a period of trial and criticism before the glossary is published in book form. Section V, *Chemical Engineering*, and Section VI, *Biophysics and Radiobiology*, both published earlier, are still in print and may be ordered for 60¢ from ASME. Section III is 75¢. The glossary is being prepared with the cooperation of scientific and technical societies and government agencies to provide standard definitions in the field. Each of the preliminary sections contains a list of all terms that will appear in the glossary, with the sections in which they will be found. Sections still in preparation are "General Terms," "Reactor Theory," "Chemistry," "Instrumentation," "Isotopes Separation," and "Metallurgy."

Miscellaneous

The IBEC Research Institute has been formed to carry on research in tropical and subtropical agriculture and related fields. This is one of several organizations formed by Nelson A. Rockefeller and his associates since World War II to aid in the development of basic resources abroad, using modern technology and management. Initial research of the institute will be on improvement of tropical agriculture in Brazil and Venezuela, with special reference to coffee techniques and the growing of rice and corn. Robert P. Russell, who resigned as vice president of International Basic Economy Corporation, is president of the institute, which is distinct from IBEC.

The German Chemical Industry: a Bibliography of the Chemical, Metallurgical and Process Industries, prepared by L. Wilson Greene for the Office of Technical Services, Department of Commerce, is one of the most complete works relating to captured technology. The bibliography contains over 2,000 references with descriptive titles or abstracts, and includes a subject index, author indexes, and cross-indexes with OTS, British, and U. S. military report numbers. Particularly helpful are sections dealing with translations and reports available from private publication services. The publication may be obtained from OTS, U. S. Department of Commerce, Washington 25, D. C., for $10.

The National Bureau of Standards urgently needs competent scientists in the fields of electronic science, engineering, and physics for research and development for the Department of Defense. The work offers opportunities for advancement and may often form the basis for a doctor's thesis. The most urgent need is for engineers and physicists at starting salaries of $4,600–$8,800. Applications are being accepted by the U. S. Civil Service Commission, Washington 25, D. C. Applications may be obtained from most first- and second-class post offices, from Civil Service regional offices, or from the commission's Washington office.

Publications Received

Proceedings of the 29th Annual Meeting, Highway Research Board. Division of Engineering and Industrial Research, National Research Council, 2101 Constitution Ave., Washington, D. C.

Procedures for Home Freezing of Vegetables, Fruits, and Prepared Foods: Classified Notes on Review of Literature. Agricultural Handbook No. 2. U. S. GPO, Washington 25, D. C. 40¢.

Fiberglas Bibliography. 3rd ed., 1950. Public Relations Director, Owens-Corning Fiberglas Corp., Toledo, Ohio.

The Utilization of Sucrose. Leslie F. Wiggins. Tech. Report Series No. 7. Sugar Research Foundation, 52 Wall St., New York 5.

Ozone and its Application in Food Preservation. A. W. Ewell. American Society for Refrigerating Engineers, 40 W. 40th St., New York 18.

Annual Report of the National Bureau of Standards—1949. NBS Misc. Publ. 198. U. S. GPO, Washington 25, D. C.

Space-Time Structure. Erwin Schrödinger. Cambridge Univ. Press, 51 Madison Ave., New York 10.

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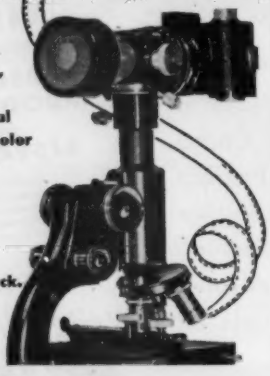

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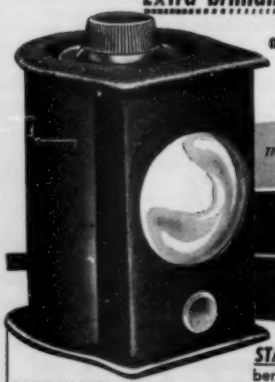

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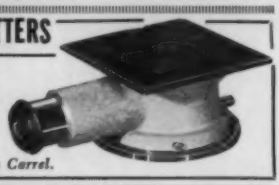

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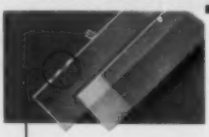

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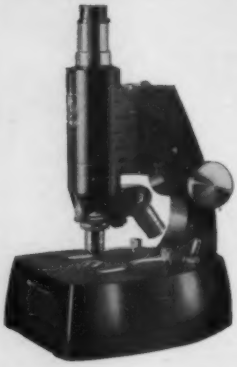

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